A STUDY ON

ASSESSMENT OF BONE MINERAL DENSITY IN OBESE AND NON OBESE DIABETICS BY THE USE OF DEXA IMAGING

In partial fulfillment of regulations
For award of the degree of
M.D (GENERAL MEDICINE)
BRANCH – 1

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The Tamilnadu Dr. M.G.R Medical University Chennai

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BONAFIDE CERTIFICATE

This is to certify that dissertation named **" ASSESSMENT OF BONE MINERAL DENSITY IN OBESE AND NON OBESE DIABETICS BY THE USE OF DEXA IMAGING"** is a bonafide work performed by Dr. K.Sivakumar, post graduate student, Department of Internal Medicine, Kilpauk Medical College, Chennai-10, under my guidance and supervision in fulfillment of regulations of the Tamilnadu Dr. M.G.R Medical University for the award of M.D. Degree Branch I (General Medicine) during the academic period from May 2010 to April 2013.

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DECLARATION

I solemnly declare that this dissertation **"ASSESSMENT OF BONE MINERAL DENSITY IN OBESE AND NON OBESE DIABETICS BY THE USE OF DEXA IMAGING"** was prepared by me at Government Kilpauk Medical College and Hospital, Chennai, under the guidance and supervision of **Dr. S. Mayilvahanan M.D.**, Professor, Department of Internal Medicine, Government Royapettah Hospital, Chennai.

This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch I (General Medicine)**.

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CONTENTS

ABSTRACT

Obesity is defined as a state of excess adipose tissue mass. In fact it is the total body fat content, which is important rather than total body weight. Diabetes mellitus is more importantly associated with obesity. Challenging the previous theory that obesity is protective against the development of osteoporosis, emerging studies had shown that obesity is detrimental rather than protective.

Aims and objectives:

To Assess the Bone Mineral Density of obese and non-obese diabetics by the use of DEXA imaging. To study the impact of obesity on bone mineral metabolism. To correlate the vitamin D levels with the BMD of obese and non-obese diabetics.

Materials and method:

A total of 50 diabetic patients included in the study. The group was subdivided in to obese and non-obese with 25 in each group based on BMI. Patients who met the inclusion and exclusion criteria were inducted in to the study. Protocols were briefed. Investigations done apart from routine were vitamin D levels. DEXA imaging done was done for all the patients.

Observations and results:

It was observed that out of 25 patients in obese group 16 were found to be osteopenic [64%] and only 3 had osteoporosis [8%].The prevalence of abnormal BMD in obese group was 80% [P <0.00] statistically significant. The percent fat mass [PFM] in obese group was 0.417 and in non-obese group was 0.286.When correlating with BMD the observation was statistically significant P<0.00. Both groups had insufficient vitamin D levels. The mean vitamin D levels in obese and non-obese were 23.1ng/dl and 27.6 ng/dl respectively. The observation of insufficient vitamin D levels was statistically significant P<0.00.

Conclusion:

It was observed that obesity is an important risk factor for the development of osteopenia in diabetics. The most prevalent type of abnormal BMD in obese diabetics was osteopenia. Both groups had insufficient vitamin D levels.

INTRODUCTION

Obesity is defined as abundance of adipose tissue mass in the body. Contrary to popular belief, obesity is not synonymous with excess body weight. In fact it is proportional to total body's fat content. Body mass index, the most commonly used measure of obesity is quantified by the formula weight in kilograms to height in meter square [weight/height^2], with a BMI of >30 is called as obesity, BMI between 25- 29.99 termed as overweight and a BMI ranging from 18.5 -24.99 is considered as normal. As obesity is considered as grade 1 failure of all organs, it is often linked to morbidity or mortality.

Diabetes mellitus is the most prevalent endocrine disorder among the world's population. India, now labeled as the diabetic capital of the world, has started feeling the brunt of the disease because of changing life style with low physical activity. Obesity and diabetes often go hand in hand, with obesity providing a substrate for insulin resistance.

Metabolic bone disease associated with diabetes mellitus is a much underappreciated complication. Of these, Osteoporosis and osteopenia are important. Diabetes is an important cause of secondary osteoporosis.

Of the available techniques the DEXA [DUAL ENERGY X RAY ABSORPTIOMETRY] imaging provides an accurate measure of bone

mineral density. It provides a cumulative score namely T- score and Z-score, with a T –score of < 2.5 indicating osteoporosis and between -2.5 and -1.0 indicating osteopenia. It also provides a quantitative measure of total body fat content in percentage. The pathogenesis of osteoporosis in diabetes mellitus is complex and controversial. Various studies have showed conflicting results portraying diabetes being protective as well as detrimental for the development of osteoporosis. The complex interplay between diabetes, obesity and osteoporosis is a matter of debate, with obesity and osteoporosis now being considered as interrelated disease because of common mesenchymal stem cell origin of osteoblasts and adipocytes.

The mechanism by which obesity in diabetes predisposes toosteoporosis is not known. However the role of leptin anappetite hormone has been forayed in to the scenario. Leptin is produced from adipocytes found abundance in obese people, through its action on β2 receptors via central sympathetic pathway, may lead to increased bone resorption. It is not known whether, the microvascular complications that occur in other vascular beds may possibly also occur in microvasculature of bone.

With this study aimed at measurement of BMD in obese and non-obese diabetics, the prevailing type of BMD in this subset of patients can be ascertained. The abnormal BMD that occurs in diabetes as a primary complication of the disease per se or as a consequence of obesity will be ascertained.

AIM OF THE STUDY

1) To assess the bone mineral density of obese and non -obese diabetic population by the use of DEXA imaging.

2) To observe the impact of obesity on bone mineral density.

3) To correlate the vitamin D levels and the BMD of obese and non -obese diabetics.

REVIEW OF LITERATURE

Osteoporosis is a common mineral bone disease characterized by, abnormality in bone architectural pattern with resultant decrease in strength and enhanced susceptibility to fracture. It is classified in to primary and secondary with the former being the most commonest.

Primary osteoporosis or idiopathic osteoporosis is seen predominantly in postmenopausal women, but can also occur in men who have underlying defects in bone formation[23].

Secondary causes of osteoporosis are related mainly with underlying endocrine disorders like diabetes, hyperthyroidism, Cushing's syndrome, Hypogonadism and obesity [54].Other pro inflammatory conditions like Rheumatoid arthritis, Anorexia Nervosa, Chronic liver and renal disease may predispose to the development of osteoporosis.

Osteoporosis is a quiescent disease till it presents with a fracture. Fracture of hip and vertebral bodies are more common in osteoporosis related fractures.

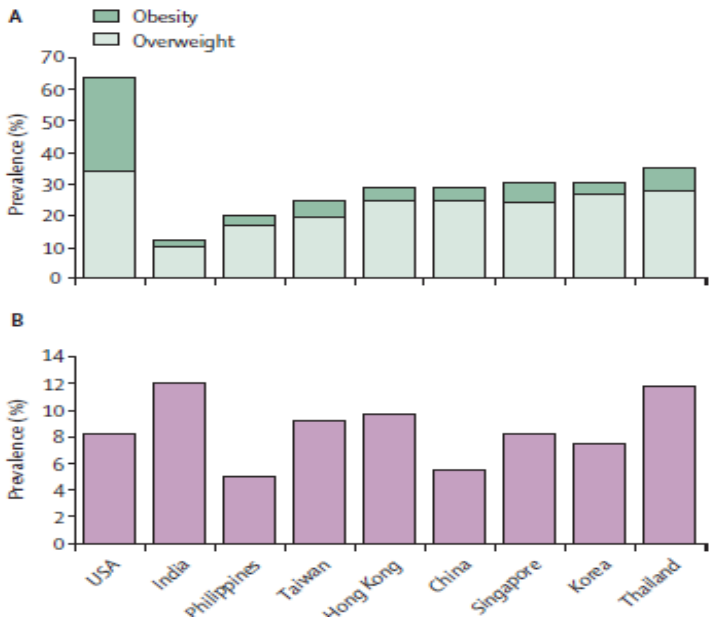
Obesity is a state of excess adipose tissue mass. Were the distribution of fat in the body is more important than the type of fat. For example, the intra-abdominal and abdominal fat is metabolically more active when compared to subcutaneous fat elsewhere. Most important complications of obesity such as insulin resistance, diabetes,

dyslipidemia, osteoporosisare related to the lipolytically active fat that are present intraabdominally.

Diabetes mellitus probably the most widely prevalent metabolic disorder among the world population .With the pandemic of disease at its peak, the knowledge of existing complications in detail and the novel underappreciated complications like diabetic bone disease is essential for the holistic approach to these common disease. Thanks to the advancement in DEXA imaging diabetes related osteopenia/osteoporosis is being diagnosed at early stages of the disease.

Prevalence of Obesity,Osteoporosis, Diabetes - World Scenario

Incidence and prevalence of obesity and osteoporosis in general population shows a considerable variation among geographical regions. National Health and Nutrition Examination Surveys data from North America had showed the obesity prevalence of 32.2% in adult men and 35.5% in adult women[23]. Data from Europe had showed that, the prevalence of obesity is maximum in United Kingdom with 12% and lowest being in Italy[77]. Among Asian countries with obesity Thailand leads the list with a prevalence rate of 6.2%[76].

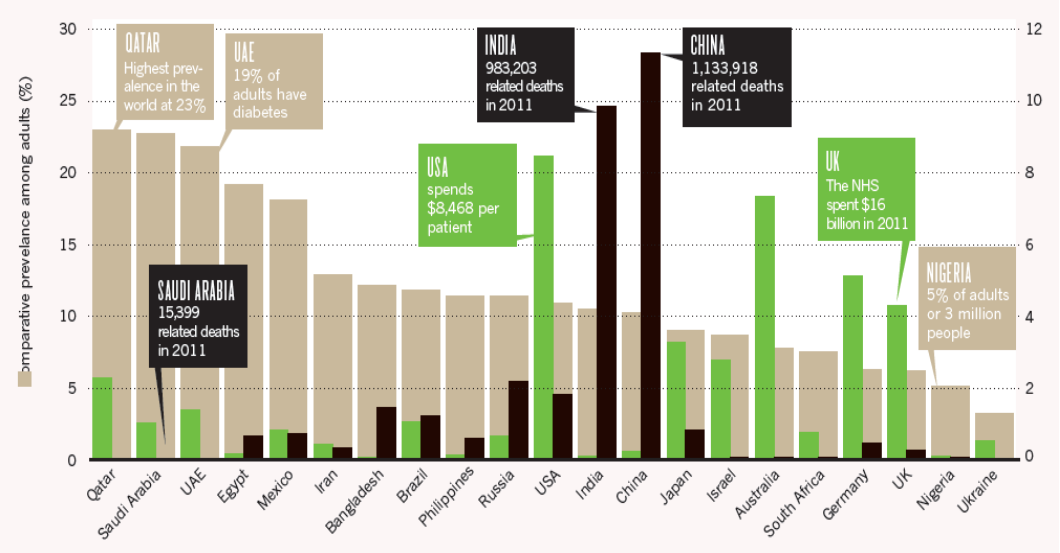


International comparison of prevalence of obesity and diabetes in adults

It is estimated that 8 million women and 2 million men in the United States are osteoporotic and additional 18 million people are osteopenic[23].The prevalence being more common in postmenopausal age group. Europe had reported maximum number of reported fractures related to osteoporosis in the world with 34.8%. The prevalence of osteoporosis in urbanized Asian countries had reached up to 30%.However the exact prevalence of osteoporosis in obesity is yet to be ascertained.

The prevalence of diabetes is 2.8% in 2000, but this figure will reach 4.4% in 2030 worldwide. The presence of generalized osteoporosis in diabetes is an underappreciated complication. Because of these along

with reporting bias the diabetic osteoporosis is less acknowledged and the data regarding its prevalence in diabetes is unknown.



WORLD WIDE SCENARIO OF DIABETES[72]

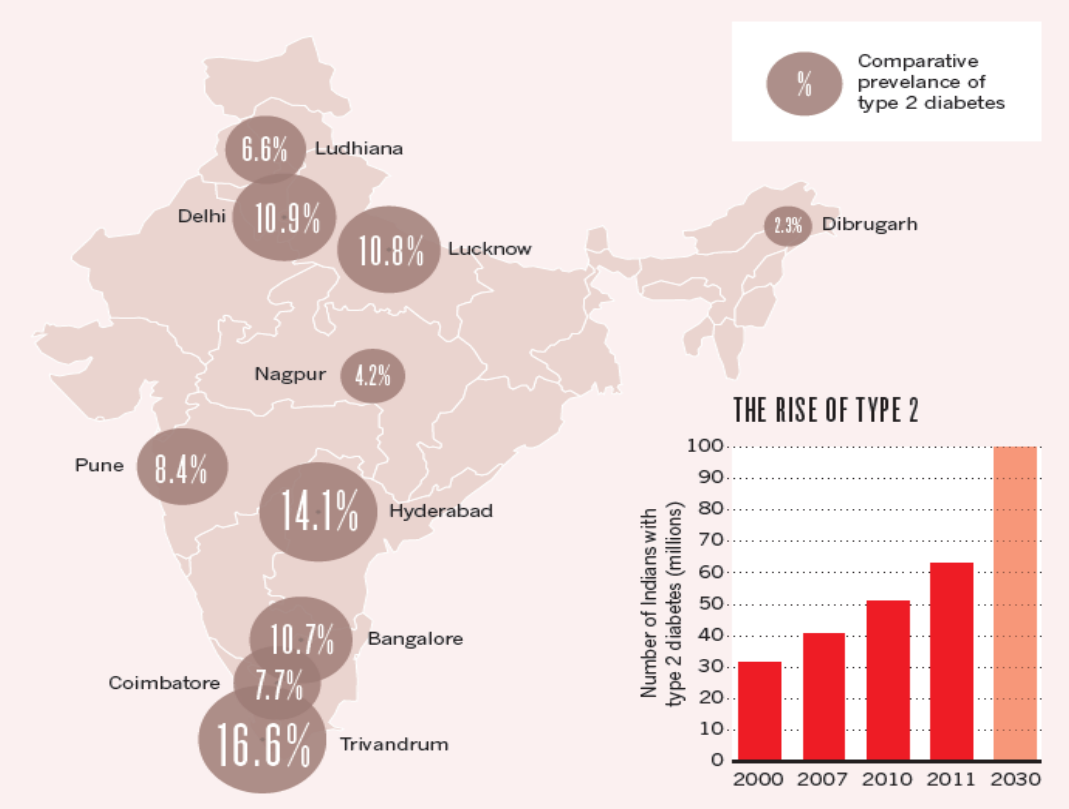
Prevalence in Indian scenario: Increasing trend

With India embracing both eastern and western lifestyle the prevalence of obesity has increased alarmingly, prevalence is between 10 and 50% in various Indian cities. One study from urban Chennai has showed a prevalence rate of 22.8% in males and 31.8% in females[74].

To the same extent with the prevalence of obesity increasing, Osteoporosis had proportionally increased. One in eight males and one in three females suffer from osteoporosis, making India as one of the largest country with osteoporotic people. The affected people with osteoporosis are set to increase by 36 million by 2013[78]. A study by Britannia New

Zealand and arthritis foundation of India had revealed that people from Kolkotta and Chennai have a prevalence rate of 45%.

As of 2011 there are 61million diabetics in India. Recent Chennai Rural Urban Epidemiological Study[CURES] had showed a crude prevalence rate of 14.3% [age adjusted],with in a span of 14 years the prevalence had increased alarmingly by 73%[75]. But the data regarding prevalence of osteoporosis in diabetics is unknown because of the under appreciation of osteoporosis in diabetics.



RISING TREND OF T2DM IN URBANIZED INDIAN CITIES AND THEIR PROJECTED OUTLOOK[73]

Demography:

The usual age of onset of osteoporosis is beyond 50 years of age, mostly confined to postmenopausal women. Male to female ratio is 1:2.66. With the increasing incidence of vitamin- D deficiency in Indian subcontinent the Indians are prone for the development of osteoporosis.

Pathophysiology of osteoporosis:

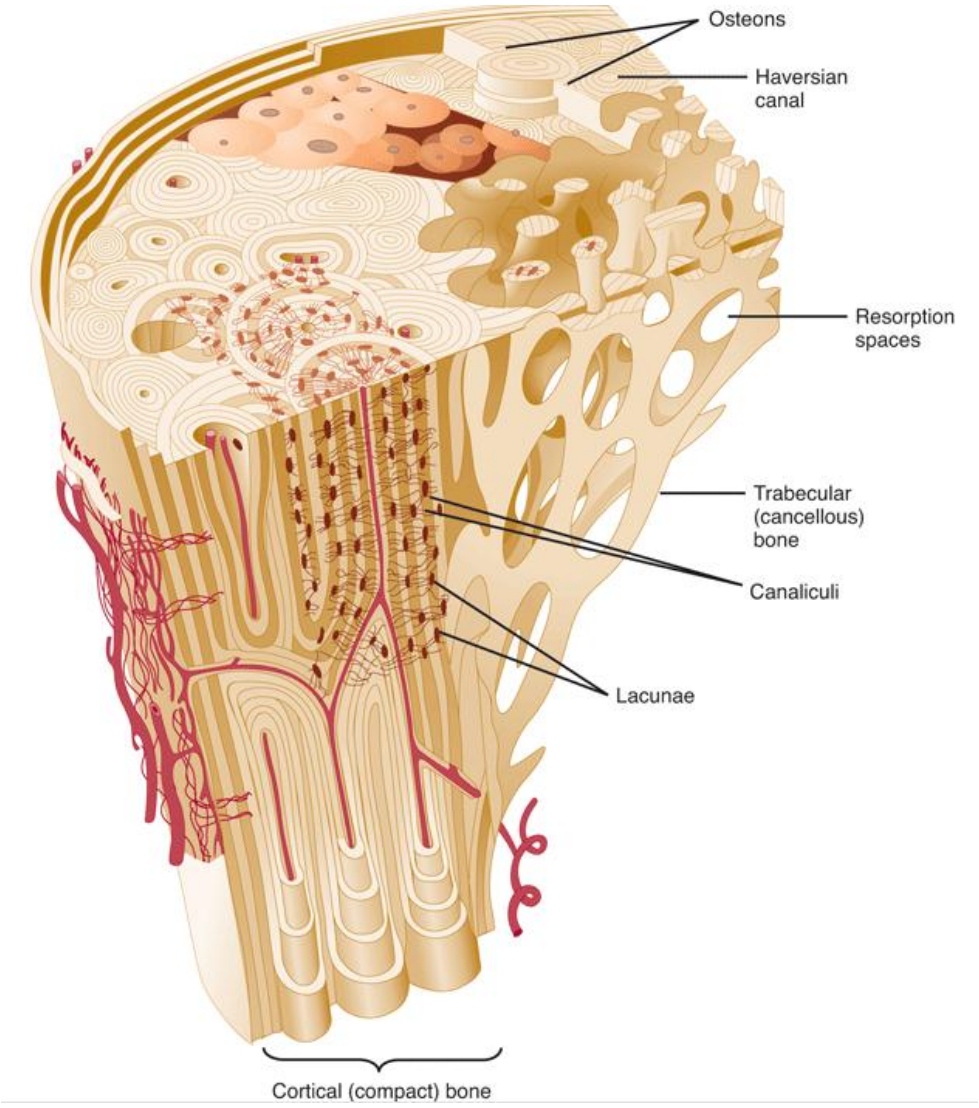
Osteoporosis is characterized by complex pathogenesis. During the period of growth till adolescence the bone formation exceeds bone resorption and after the age of 30 years the bone resorption tends to exceed formation[1].The bone loss after menopause increases to 2-3 percent per year as compared to premenopausal bone loss[1]. With cancellous bone being more metabolically active it bears the major brunt of the disease. The bone makeover has been linked with polymorphisms in the gene for vitamin D receptor(VDR)[2]. In addition polymorphisms in gene coding for estrogen receptor α (ERα) has been associated with some determinants of accelerated postmenopausal bone loss in women[3].

The basic pathogenic mechanism in osteoporosis is excess skeletal tissue fragility which can result from:

1) Production of skeleton with decreased mass and endurance during childhood and puberty [4].

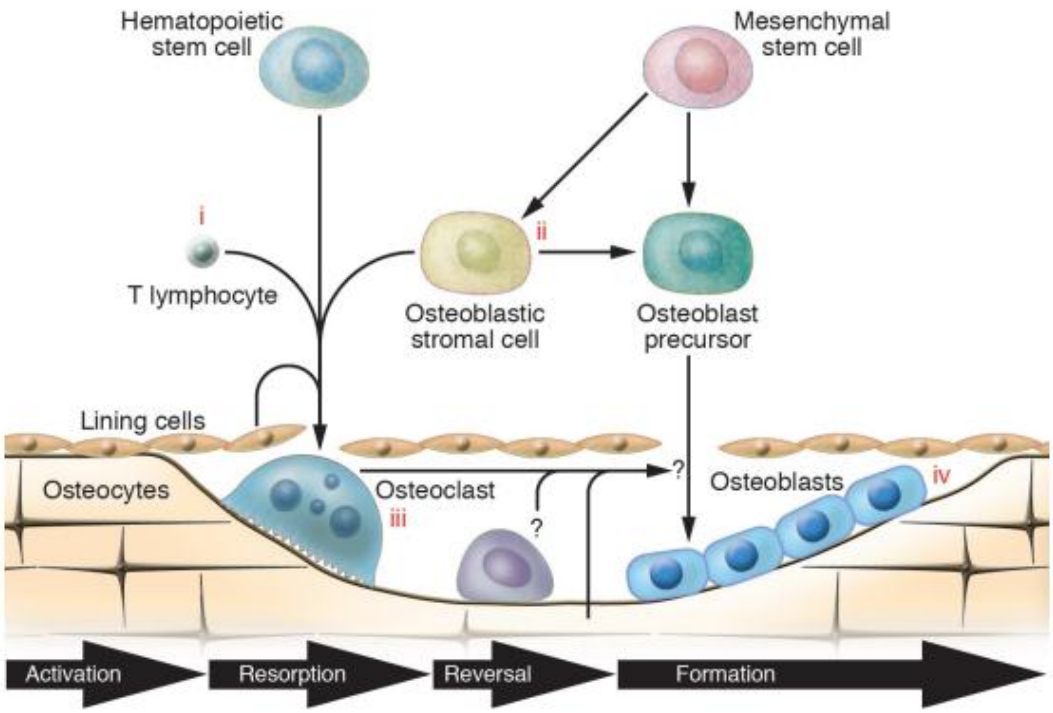
2) Enhanced bone resorption leading to decremental bone mass and distortion of architectural pattern of bone[4].

3) Deficient bone formation response[4].



COMPACT BONE SEEN IN HORIZONTAL AND VERTICAL SECTION

In order to realize, how an exuberant skeletal resorption and deficient bone formation result in osseous fragility, it is prudent to perceive the physiology of remodeling process of bone, a phenomenal accomplishment by the bone cells of matured skeleton.

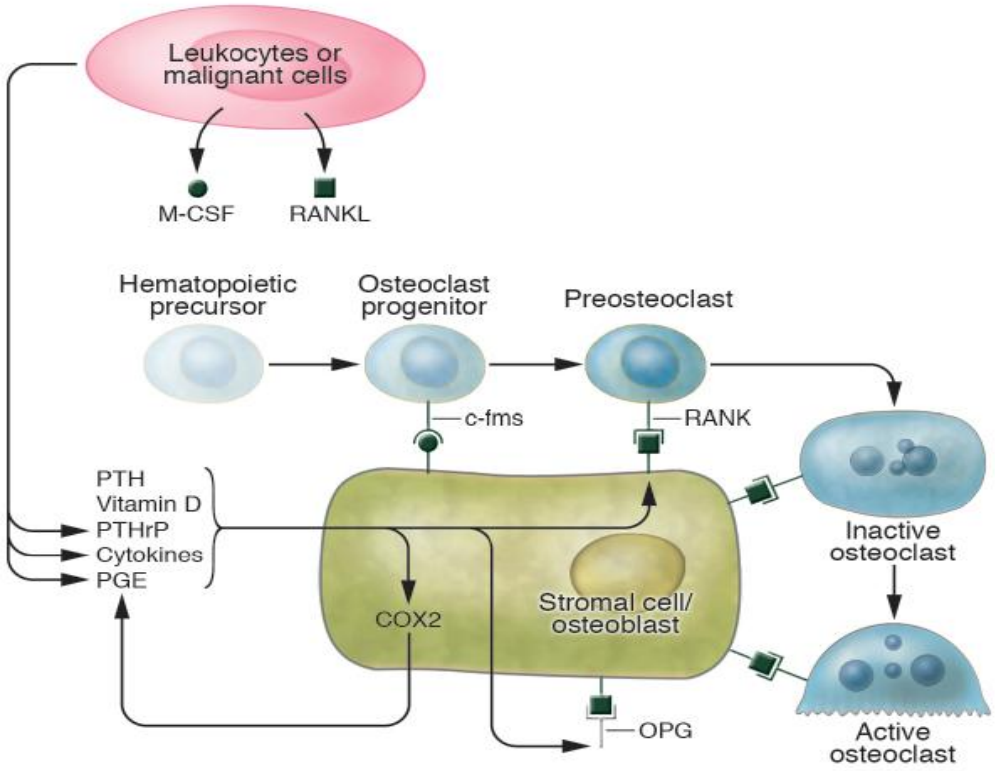


MECHANISM OF BONE REMODELING

Bone remodeling involves two imperious processes. First maintains skeletal strength by repairing micro damage to bone. Second constant supply of calcium to maintain blood calcium levels[23].

The remodeling process or bone multicellular units (BMUs) was first delineated by Frost and colleagues[5] can occur either on the surface of cancellous bone as discontinuous Howship lacunae or secondly in the

cortical bone as an regular cylindrical Haversian systems. As depictedin the Figure remodeling starts with the stimulation of hematopoietic stem cells to differentiate in to osteoclasts. Two important cytokines needed for osteoclastogenesis are M-CSF(macrophage colony stimulating factor) and RANKL (Receptor Activator of Nuclear factor κβ). The receptor for RANKL is RANK and is expressed on the precursor cells of osteoclasts [15]. Osteoprotegerin (OPG) is a decoy receptor for RANKL and opposes the osteoclastogenic action of RANKL[15].



REGULATION OF OSTEOCLASTIC FUNCTION

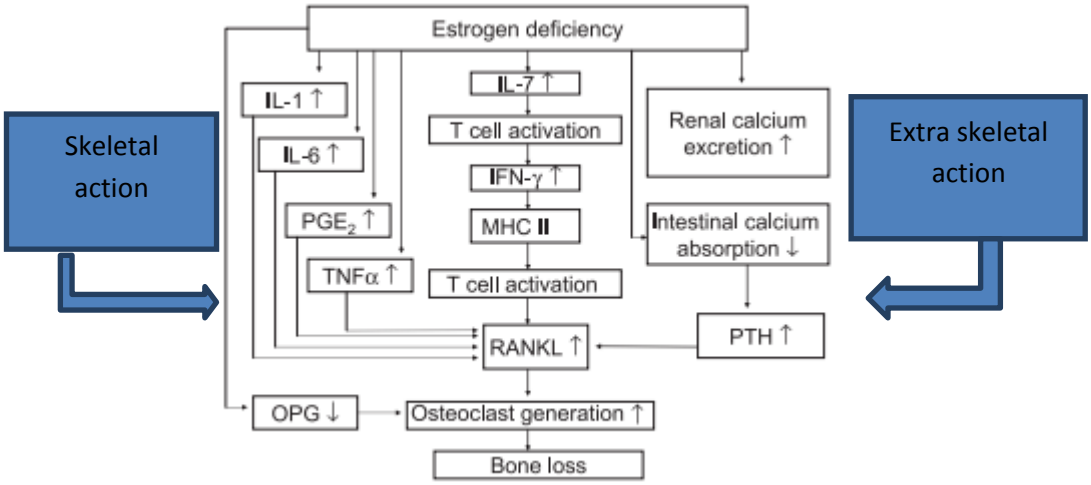
In this complicated remodeling process, the initial step will be the interaction between osteoblastic and osteoclastic cell lines. Macrophage-Colony Stimulating Factor incorporates with its receptor, c-fms, to activate the proliferation as well as the differentiation of hematopoietic progenitors, which then express RANK as preosteoclasts. Osteoclast are stimulated by RANK/RANKL interaction, and this interaction is inhibited by osteoprotegerin(OPG). The COX2 activity is stimulated by bone resorbing factors which in turn produce prostaglandins and amplify the responses to RANKL and OPG. In pro inflammatory states, osteoclastogenesis may be increased by production of soluble or membrane bound M-CSF and RANKL along with PTH-related protein (PTHrP), cytokines, and prostaglandins[4].

These freshly differentiated osteoclasts needs an interplay with osteoblastic cell line. With osteoclasts holding center stage in the resorption phase, which is of shorter duration followed by reversal phase in which bony surface is encased by mononuclear cells. The osteoblastic replacement process takes a longer duration in which osteoblasts actives lay matrix over the scalloped surface produced by osteoclasts[4].Whereas the resorption and reversal phases of remodeling requires a shorter duration, so any augmentation in the speed of remodeling process will lead to bone loss. With the number of under filled Howship lacunae and Haversian system increasing the strength of bone will be weakened proportionally [4].

Enhanced resorption process leads to complete loss of trabecular structures, leaving no substrate for new bone formation. These are the various ways in which an increase in resorption function of osteoclasts can lead to brittleness of bone. Not always, high rates of resorption will lead to bone loss; one classical example being the pubertal growth spurt. Therefore deficient bone formation during the process of remodeling is an pivotal component in the pathophysiology of osteoporosis[4].

Pivotal role of estrogen:

It’s a well-known fact that estrogen deficiency will leads to bone loss, as evidenced by increased prevalence of osteoporosis in postmenopausal age groups. Studies had proved that, bone remodeling process is accelerated at menopause as evidenced by the increased level of biomarkers for resorption and formation after menopause[6].



Mechanism of estrogen deficiency leading to bone loss

In contrary to Albright's original hypothesis, the surge behind the bone loss in the light of estrogen deficiency is increased bone resorption and not impaired bone formation. Estrogen is both anti-catabolic and anabolic, suggested by the fact that the normally occurring increased bone formation response to mechanical loading, fails to occur in estrogen deficiency[7].

The amount of estrogen required to inhibit the resorption is less than one fourth that is needed for the growth of breast tissue and uterus[8]. Estrogen is required for epiphyseal closure in men and women. In addition, the lower estrogen levels are the most important cause of osteoporosis in older men than low androgen levels[9].Estrogen has skeletal and extra skeletal activities, in skeletal action it has direct and in direct action. Direct action is mediated via estrogen receptors in osteoclasts and osteoblasts. The indirect effects are mediated via its

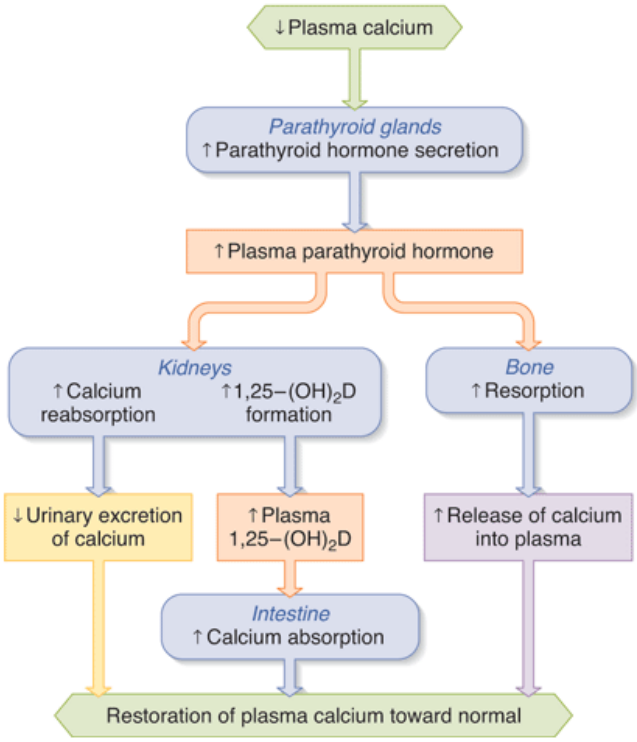
action on estrogen receptors on stromal cells. Estrogen deficiency will lead to increased expression of RANKL on bone marrow stromal cells, which is important for bone resorption[16].Estrogen itself stimulates Osteoprotegerin(OPG) production in osteoblasts and antagonizes resorptive effects on bone[17]. The extraskeletal manifestations are increased renal calcium excretion and inhibition of calcium absorption from gut, these effects may lead to secondary hyperparathyroidism, in addition estrogen has suppressive action on parathyroid hormone levels[18].

Estrogen exerts its action via two receptors ERα and ERβ. The ERα is most important for its action [4]. Estrogen induces osteoclast apoptosis via TGF-β production [10]. It also reduces the amount of reactive oxygen species[11].The osteo immunology behind estrogen deficiency is the increased production of IL-7, this in turn activates T cells. T cells in turn expresses TNF-α and INF γ and leads to over expression of MHC (major histocompatibility complex) class 11molecules on the surface of bone marrow stromal cell which further leads to more production of T cells and production of RANKL and TNF-α, both are pro osteoclastogenic.

Role of vitamin D, calcium and parathyroid hormone:

Calcium deficiency that results from either decreased intake or deficient absorption from intestine secondarily due to disease per se or

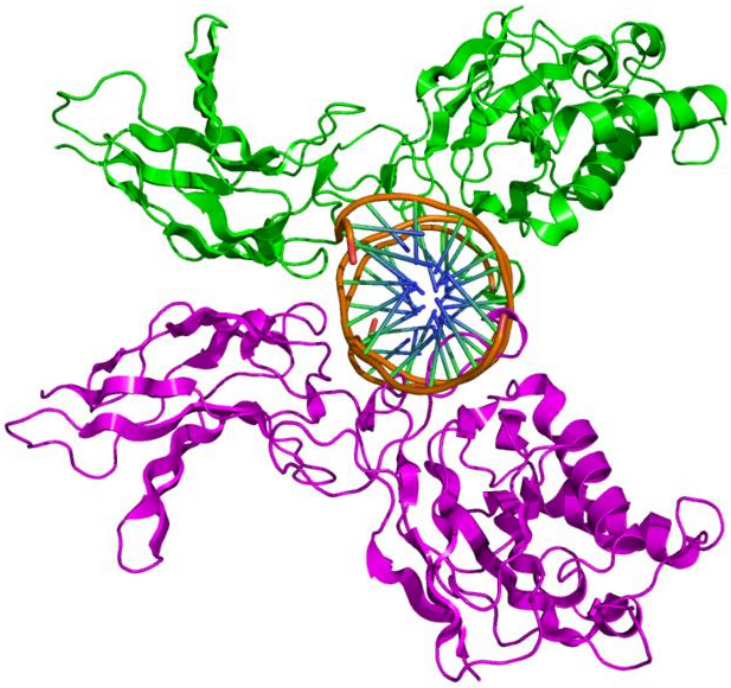
due to aging along with vitamin D deficiency leads to secondary hyperparathyroidism[4].Vitamin D3 is needed not only for absorption of calcium from the small intestine but also for its negative influences on paratharmone[12]. Vitamin D deficiency and secondary hyperparathyroidism leads not only to increased bone loss and skeletal fragility, but also to increased frequency of falls which is more common in diabetics [13,14] probably due to neuromuscular impairment. Various trials had proved that vitamin D supplementation along with calcium in elderly people will results in increased bone mass along with reversibility of falls.



Interrelation ship between parathyroid hormone, Vitamin D and calcium

Secondary hyperparathyroidism is commonly seen in patients with vitamin D insufficiency which is defined less than 30 ng/ml, hence forth the target vitamin D levels should be more than this level[19]. There is a seasonal decrease in vitamin D levels along with elevated levels of parathyroid hormone. There is also increased risk of cardiovascular mortality in people with secondary hyperparathyroidism, the mechanism behind this is unknown[20].

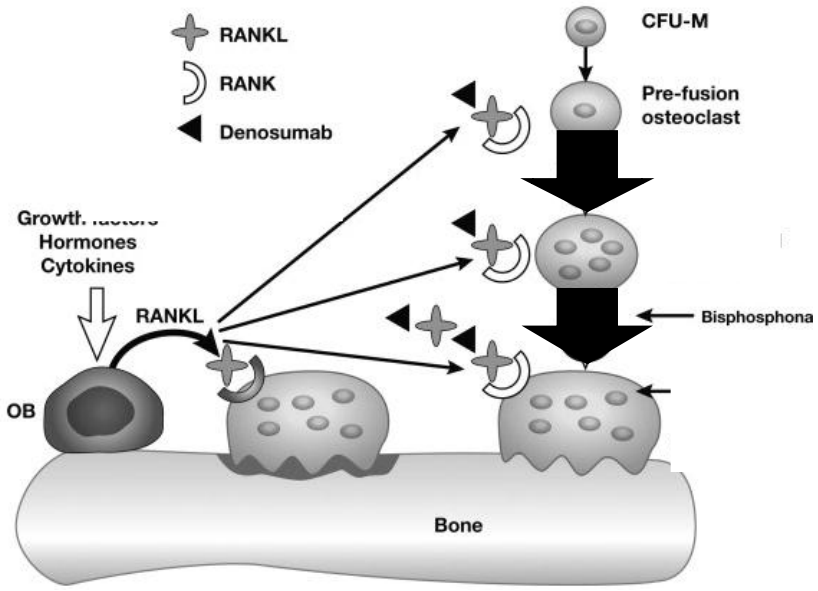
Receptor Activator of Nuclear Factor-κβ:



X RAY CRYSTALLOGRAPHIC STRUCTURE OF NF-κβ

The Molecular mechanism behind the interaction between osteoblastic and osteoclastic lineages has been found recently[21]. The cytyokines responsible for this interaction belong to TNF (Tumor Necrosis Factor) family of receptors. Receptor activator of Nuclear Factor- Kβ is on hematopoietic cells, which is responsible for osteoclastic differentiation and function. RANKL/RANK interaction is necessary for bone resorption. Osteoblasts also secrete osteoprotegerin(OPG) which is a decoy receptor for RANKL/RANK interaction over expression of OPG knockout transgenic mice leads to development of Osteoporosis[22].

Recently a possible second system may be involved the interaction between osteoclastic and osteoblastic lineages, these are the Fc receptor common γ chain and membrane adapter DNAX-activating protein 12[4]



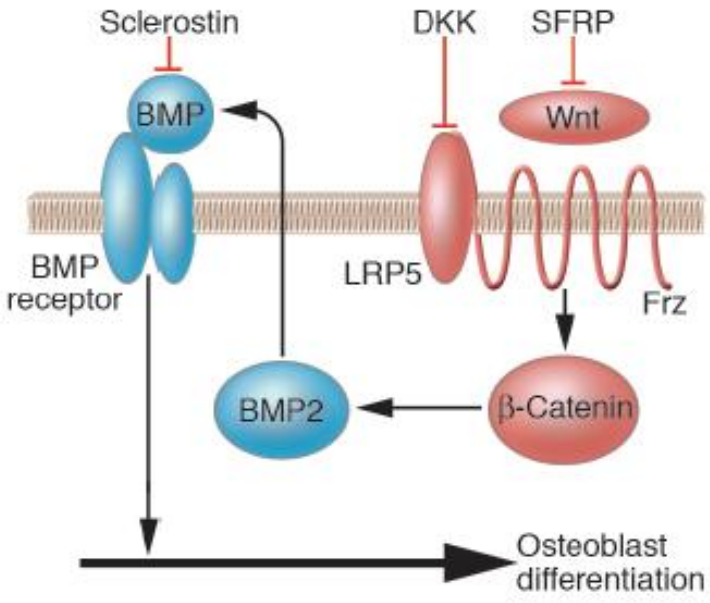
Final common pathway that is altered in the pathogenesis of osteoporosis

Genetics in osteoporosis:

The signal transduction pathways and transcription factors necessary for osteoblastic activity had shown several novel pathways to decipher and to understand the pathophysiology of osteoporosis[4].Studies had suggested that a genetic locus on chromosome 11 is associated with high bone mass. Recent Gene deletion studies have demonstrated that absence of runt-related transcription factor 2 (Runx2) or osterix, are critical for osteoblast differentiation[24].The second fiddle played by the Wnt signaling pathway in controlling osteoblast activation is of great interest to researchers, and it was recently identified it plays an important role in determining bone mass and strength [4].

The ***wnt*** signaling pathway is a network of messenger system that transfer the information from the cell surface to the nuclear DNA.

LDL Receptor related protein 5 (LRP5) communicates with the frizzled receptor to transfer the message through Wnt ligands. Any mutation of LRP5 that leads to activation of wnt pathway at a constant rate will culminate in an increased bone mineral density [25].Deletion of *LRP5 gene will* result in osteoporosis along with abnormality in the eye movements. Loss of function mutations in the gene coding for LRP5 is seen in few of the patients with idiopathic juvenile osteoporosis.



Wnt pathway, BMP AND SCLEROSTIN

Osteoblastic functional evolution depends on the functioning of wnt and BMP pathways. The signaling through wnt requires the interplay between LDL receptor protein 5 and the frizzled receptors (Frz) and in turn this interaction can be inhibited by Dickkopf (DKK; an inhibitor of LRP5) and secreted frizzled related protein (SFRP). Antagonists such as sclerostin blocks both the BMP and Wnt signaling. The β-catenin can form an alliance with BMP2 to intensify the osteoblastic function.

The Wnt signaling pathway is crucial to responsiveness of the effects on mechanical loading on bone [27].Wnt signaling can affect the peak bone mass [28].

Glucocorticoids mediates its effect on skeletal structure through Wnt signaling [29].There is an association between bone mineral density with the occurrence of osteoporosis related fractures and polymorphism in the genes encoding IGF1 and TGF-β [30],but a study from Icelandic and Danish cohorts, shows that polymorphisms involving*BMP2 (bone morphogenic protein)*gene are associated with low BMD and fracture risk [31].Local production of IGF-1may be the cause ascribed to glucocorticoid-induced osteoporosis as also to the growth inhibition in childhood[29].

Role of inflammatory mediators:

The chemokines such as interleukin -1(IL-1) and prostaglandin E2 (PGE2) can affect bone remodeling process[32]. Prostaglandins have both agonistic and antagonistic effects on bone. However, the most important action of PGE2- the most abundant prostaglandin synthesized in skeletal tissue, is to enhance bone resorption and subsequently bone formation [33]. The fact that these chemokines may play an important role in the evolution of osteoporosisis proved by experimental models of skeletal loss after gonadectomy[34]. The genetic polymorphisms of interleukins 1, 6 and tumor necrosis factor α and their receptors can affect the osseous mass in humans [4].

PGE2 is synthesized in bone cells mainly by the effect of inducible cyclooxygenase 2 (COX2).Cyclooxygenase is stimulated by the factors that may also induce resorption of bone and may augments the riposte[35].Treatment with Cyclooxygenase blockers decreases the response to mechanical effects of weight bearing and fluid shear stress. Prostaglandins have pivotal role to play in response to weight loading, and this effect is augmented by estrogen [36].

In addition to endothelial cells, NO synthesized in bone cells is an important cofactor for the growth response of bone to weight bearing[4].NO inhibits bone resorption, possibly by increasing OPG production there by having opposing action to PGE2[37]. This may be the possible reason for the enhanced Bone Mineral Density that is seen in patients on nitrates and various

NO pathway activators [4].Leukotrines the products of lipooxygenase cascade can also influence the bone remodeling by enhancing bone resorption and blocking the bone formation process[38].

Matrix abnormalities- A Novel hypothesis:

Recent investigations had proved that polymorphisms in gene coding for α1 chain of type 1 collagen along with hyperhomocystenemia will lead to fracture risk that is independent of BMD, probably due to difference in collagen cross linking and helix formation[39].

Leptin and other neural pathways:

Leptin is the appetite hormone. Mice knocked out with leptin gene had higher BMD than Mice with leptin gene, suggesting the role of obesity as important risk factor for the development of osteoporosis. As adipocytes are the major source of leptin, it mediates it action via central adrenergic action [40]. The role of leptin is discussed in detail in the section of obesity and osteoporosis.

OBESITY A NEW RISK FACTOR FOR OSTEOPOROSIS?

In the era of evidence based medicine, what holds true today may not hold for tomorrow. This is very much applicable for obesity. The old concept that obesity is a protective factor for the development of osteoporosis is no longer holds true. Recent studies had clearly proved that obesity is not protective and in fact it is detrimental for the development of osteoporosis[41,85-87].

The primary action of skeletal framework is to offer a tough core to back up, preserve, and promote the activities of soft tissues. Ribs, skull and pelvis safe guard their contents. The ribs will be essential for thoracic movements, like wise femur and tibia are important for ambulation. Therefore it is credible from maturation point of view, that the skeletal framework's endurance would be closely related to soft tissue mass. If all humans had the similar sized skeleton irrespective of their body weight,

few maybe at disadvantage of having bones that were inefficient to perform the task, and few might be having a heavier frame of skeleton than it need to be.

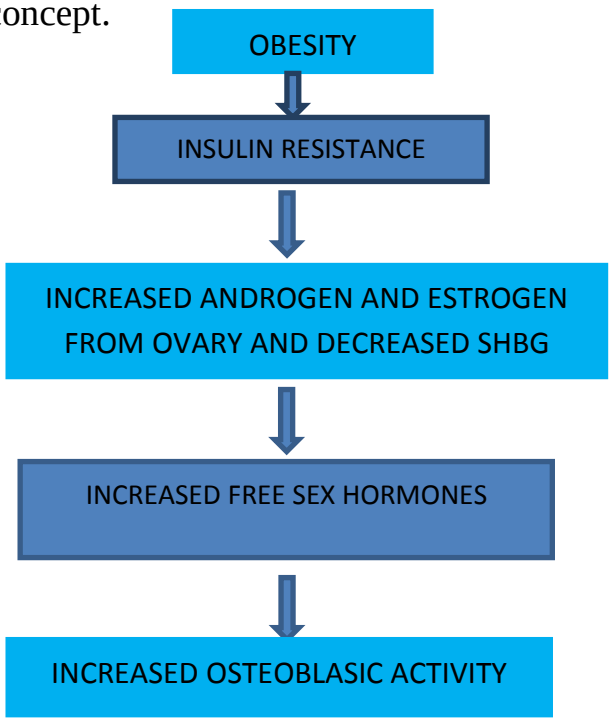
Body weight is a composition of lean mass and fat mass[41]. It should be emphasized that, the simple correlation between lean body mass and mineral content of bone tends to overestimate the relationship BMD and muscle mass[42]. Muscle mass and bone mineral content are conspicuously depends on height, but the bone density is an independent variable that does not depend on height. Simply, longer legs in taller individuals have larger muscle mass to cover them. Hence larger mass imparts a greater mechanical loading on the bone. Emerging studies are now concentrating on new variable called percentage fat mass. Bakker et al[63]found that fat free mass had correlated positively with lumbar bone mineral content over 10 year follow up period in young subjects. Because fat free mass [FFM] can be accounted as a proxy for skeletal muscle mass. Observation from bakker et al indicate that the importance of muscle contractions to increase bone strength in the study population[63].

Review of existing concepts about obesity and bone mass:

It has been proved from the vast available epidemiological data that the excess bodyweight will result in a high bone mass, so reduction in the weight may lead to bone loss [44,45,46]. The physiology behind this interrelationship is not clear, although several plausible reasons have been advocated. It is an accepted hypothesis that heavier the body mass bigger

will be the impact of shear stress on bone and that bone mass increases proportionately to accommodate the load. In postmenopausal women the major source of estrogen is adipocytes. Estrogen by blocking the activity of osteoclasts inhibits the resorption process. The argument being any increased adiposity will increase the body mass index in postmenopausal women. This effect may translate into decreased osteoclast mediated resorption with resultant increase in bone mineral density[47].

Obesity leads to insulin resistance and increased insulin levels causes an increased synthesis of androgens as well as estrogen and decreased production of sex hormone binding globulins by liver which in turn causes increased levels of free sex steroids and stimulation of osteoblastic activity by sex steroids. Recent developments in science had questioned this concept.

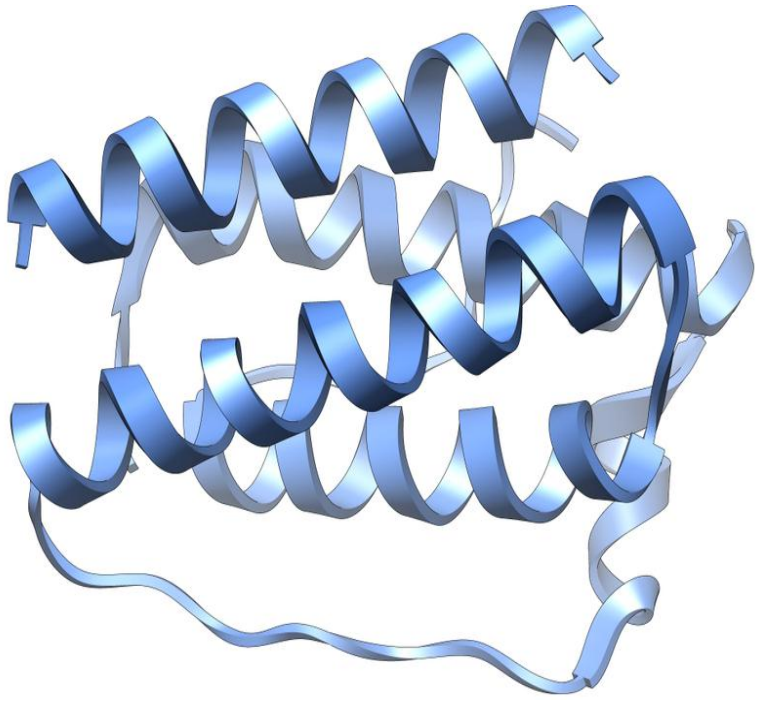


RELATIONSHIP BETWEEN OBESITY, INSULIN RESISTANCE AND BONE HOMEOSTASIS

The relationship is far more complex as thought between these variables. The discovery of appetite hormone leptin and its role in energy metabolism had thrown light on its influences bone metabolism[51]. Ducy et al had reported that leptin receptor and leptin deficient mice had showed increased bone formation. Leptin-deficient and wild-type mice had showed bone loss when leptin was injected to cerebral ventricles[51].

LEPTIN- ROLE IN OSTEOPOROSIS:

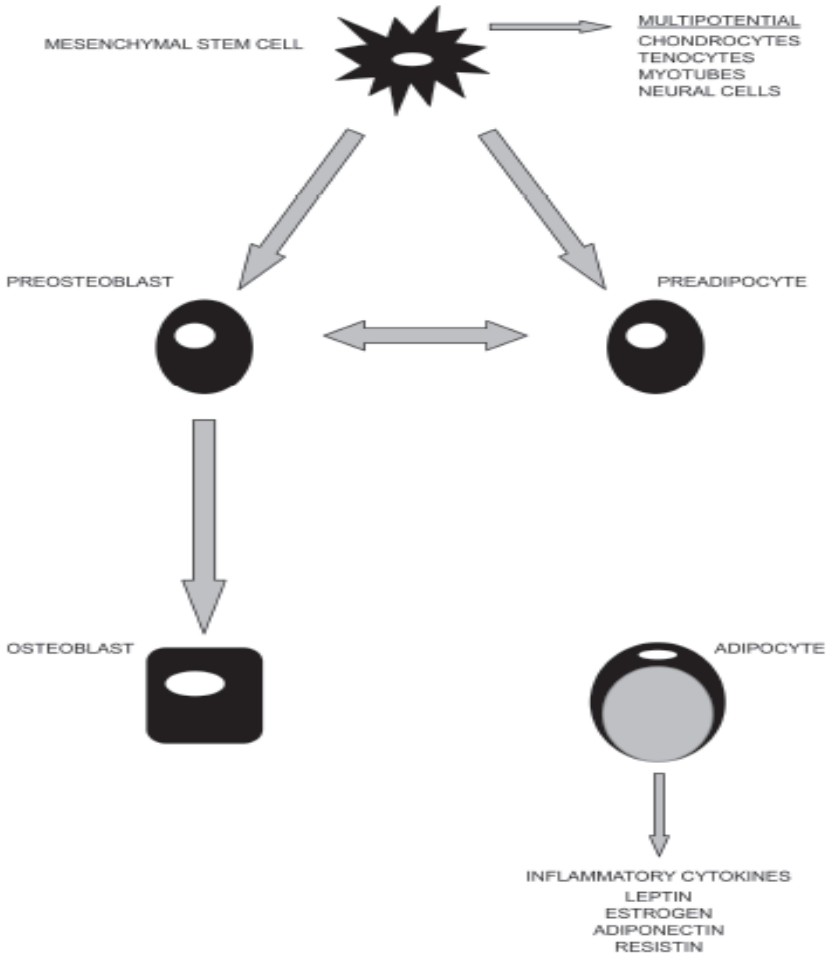
Leptin meaning thin is a 16-kDa protein , called as satiety hormone plays a very crucial role in regulating energy intake and expenditure including gappetite/hunger and metabolism. It is an adipose tissue derived hormone. The leptin gene is located on chromosome 7 in humans[52].



CRYSTALLOGRAPHIC STRUCTURE OF LEPTIN

Human leptin has 167 amino acids. It is synthesized primarily from white adipocytes, and the amount of leptin circulating in plasma is directly proportional to the total body fat content. The other sources of leptin are from brown adipose tissue, skeletal muscle, fundic glands, syncytiotrophoblasts of placenta, ovaries, mammary cells, pituitary, liver and bone marrow[53].

The fact obesity and osteoporosis are interrelated disease can be explained by the fact that both adipocyte and osteoblast arises from common mesenchymal cells[55]. Mesenchymal cell upon its differentiation is committed for pre-osteoblasts and pre-adipocyte. But upon stimulation by the cytokine called Peroxisome Proliferator Activated Receptor(PPAR-γ) the mesenchymal stem cell is more committed towards the differentiation in to adipocyte. Hence further, adipocyte expresses its hormones like estrogen, leptin, adiponectin and resistin[55].



Physiology behind the adipocyte differentiation

Adiposity signal:

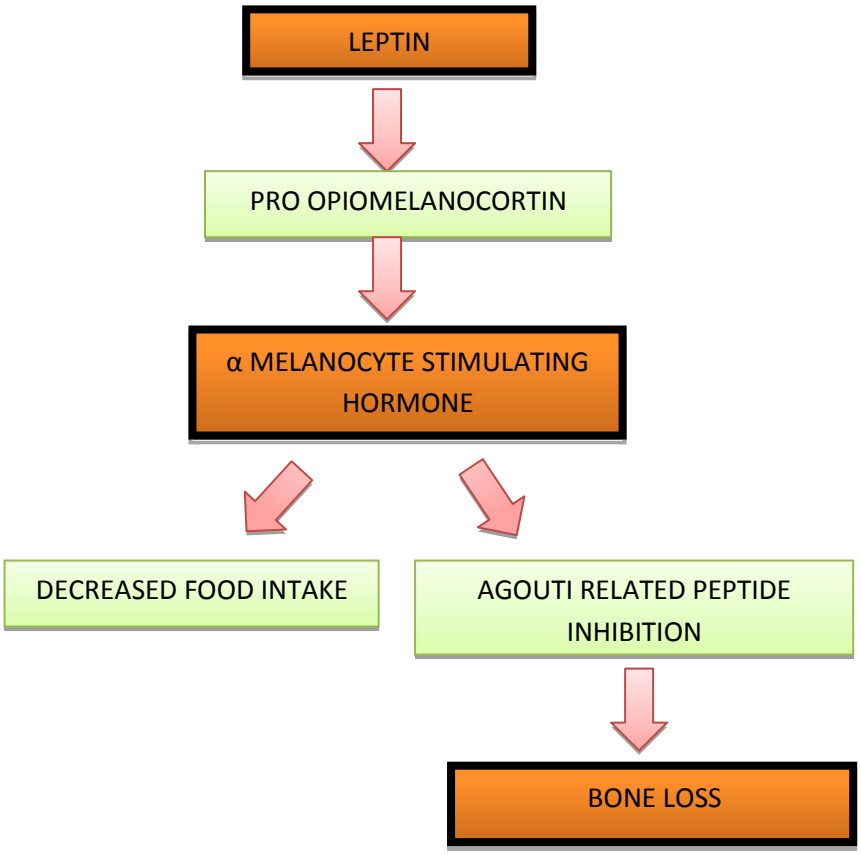
Till date, only insulin and leptin are known to act as adiposity signals. In general,

- Circulating leptin levels parallels body fat content.
- Proportional to its plasma concentration it enters central nervous system.

- Leptin receptors are found in central nervous system neurons and appear to play a major role in maintains the energy intake and output.

- Controls energy expenditure and food intake through its action on medial basal hypothalamus.

Leptin mediates its effect on bone through central sympathetic action[54]. The central sympathetic action involves both catabolic and anabolic pathways. Physiologically the catabolic pathway seems to have a major effect on the bone metabolism[54].

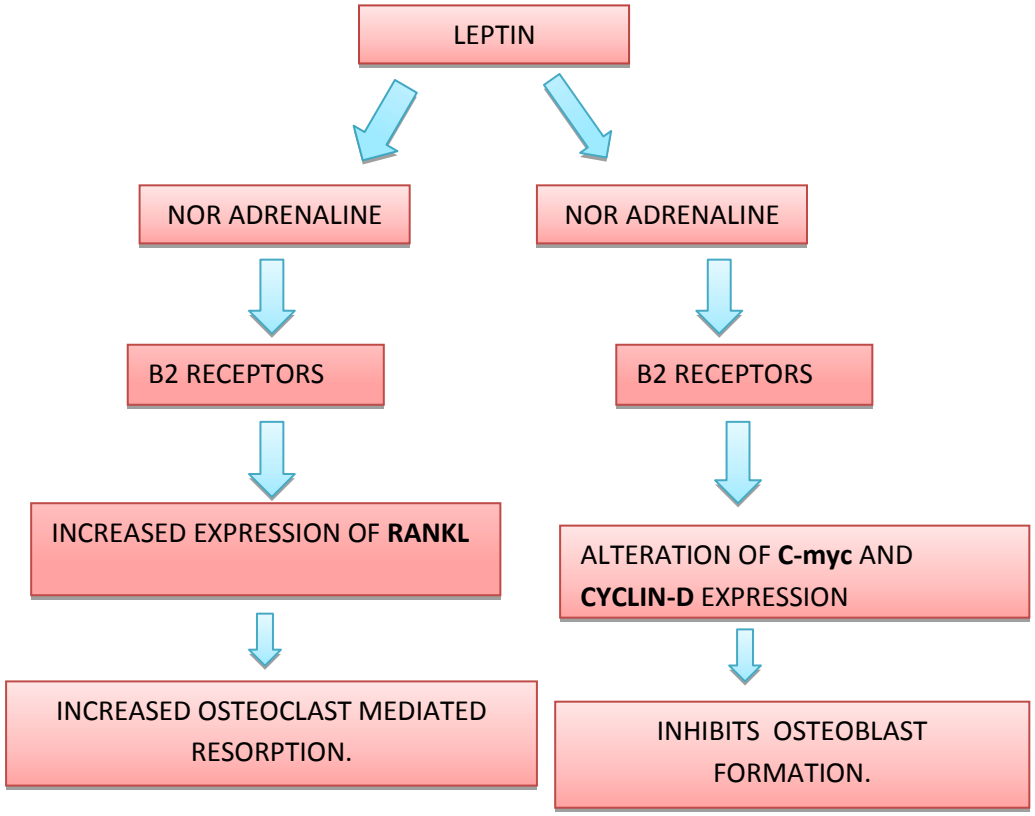


CATABOLIC PATHWAY LEADING TO BONE LOSS

Leptin via its action through pro-opio melanocortin leads to stimulation of α-melanocyte stimulating hormone(α- MSH). α- MSH exerts its action via two melanocortin receptors MC3R and MC4R. Leptin by inhibiting agouti related peptide which is are endogenous antagonist to melanocortin receptor leads to bone loss[55].

Sympathetic effects of leptin:

To emphasize the Original study from Ducy et al[51] which showed bone loss in mice infused continuously with leptin leads to bone loss. Though leptin has both positive and negative effects on the bone, it's the positive effect that is more important in vivo[55].



EFFECTS OF LEPTIN ON SYMPATHETIC PATHWAY IN CNS

Leptin via its action on β2 receptors which is mediated by noradrenaline increases the expression of receptor activator of Nuclear Factor κβ [NF-κβ] mediated via phosphorylation of protein kinase A pathway. Therefore it increases the osteoclast mediated bone resorption. In addition via the same pathway it causes alteration in c-myc expression leading to inhibition of osteoblast mediated bone formation[55].Leptin receptor–deficient *db/db* mice and Leptin-deficient *ob/ob* mice are extremely obese[56]. Some studies had proved direct effect of leptin on cortical bone formation but not on cancellous bone.

Role of other adipocyte derived hormones:

In addition to leptin, the adipocyte derived hormones are important in influencing bone mineral metabolism.

Adiponectin :

It is an adipocyte derived hormone that has anti-inflammatory and anti atherogenic effect [57], apart from energy metabolism and bone homoestasis. In contrast to leptin levels which are elevated in obesity, adiponectin levels are suppressed in obesity and also in diabetics[55]. Its receptors are seen in

Primary human osteoblasts[58].Pioneering studies from LenchikL et al had proved an inverse relationship exists between bone mineral density and serum adiponectin levels[58]. Subsequent studies had shown

conflicting results, clearly indicating further studies are needed to undermine the role of adiponectin and its influence on bone metabolism.

Resistin:

Resistin, an adipocyte-secreted factor discovered recently. This Hormone was discovered during a screening process in patients with oral hypoglycemic agents (insulin sensitizing drugs) for an unknown substance which was down regulated in diabetics. It has been claimed to be associated with diabetes and obesity [59]and the serum resistin levels were elevated in proportion to the degree of obesity[59].Thommesen et al [60] had showed resistin may mediate an important effect on remodeling the bone. Resistin is expressed in osteoblasts, osteoclasts and bone marrow cells and they help in cytokine expression, osteoblast proliferation, and osteoclast differentiation[60].Oh et al studied the relationship between serum resistin levels and bone mineral density. They found converse relationship between serum resistin levels and BMD of lumbar spine in adult men, but they found out that variance was small[61].

Brief view on other hormones that influences obesity and BMD:

Insulin:

Obesity is synonymous with Insulin resistance and numerous studies had underscored the fact that insulin is an important orchestrator in bone metabolism. The Fasting levels of insulin were correlated

affirmatively with BMD of middle-aged women [55]. Similar correlation was shown in both sexes in other studies. Tuominen et al [62]showed that individuals diabetes have reduced BMD compared with normal individuals. Contrasting studies have revealed insulin may aid the protective effect of obesity. Elevated insulin levels in obesity is because of resistance and related with overproduction of estrogen, androgen and diminished synthesis of sex hormone-binding globulin by the liver [4].The unbound sex hormones leads to suppressed osteoclastic and enhanced osteoblastic activity culminating in high bone mass[4].But these finding is not reproducible in recent studies. Like the complicated relationship between fat and bone, so is the relationship between insulin and bone that is too complex to understand. The fact that obesity is sometimes called as diabesity is because, only 10% of obese people suffer diabetes on the contrary most of the diabetics are obese. The paucity of insight in the continuum of obesity may be the fact behind the discrepancies in the literature with regards to the fat and bone relationship [55].

Amylin:

Amylin is co-secreted along with insulin. It is a 37-amino acid peptide, a member of the calcitonin family of hormones.The obese individuals have higher basal amylin levels when compared with controls [55].By its central and peripheral mechanisms amylin infusion seems to decrease food intake and has capacity in attenuating body fat and weight.

The increased amylin levels in obesity leads to down regulation of amylin receptors and dampens the effect of amylin secretion on gastric emptying and satiety. Amylin has been shown to suppress osteoclast development there by inhibiting bone resorption.

The net effect is high amylin levels in obesity leads to high bone mass[55].

Preptin:

Preptin is a 34-amino-acid peptide hormone secreted from β cells of Pancreas, Corresponding to Asp- Leu of the proinsulin-like growth factor II(proIGF-II) E-peptide. Circulating levels of preptin are elevated in obesity[55].It is co-secreted with amylin and insulin from the pancreatic βcells. The Cornish et al[63]focused on preptin's effects on bone and they proved that preptin is agonistic to bone growth in vitro as well as in vivo. But the fact is, it does not influence the osteoclast activity.

Diabetes and osteoporosis:

Diabetes mellitus is a pandemic endocrine disorder with substantial morbidity and mortality. The skeletal manifestations of diabetes mellitus are

1) Diabetic foot syndrome.
2) Charcot's arthropathy and the much under appreciated
3) Osteopenia and osteoporosis.

Osteoporosis is the most outstanding metabolic bone disease in diabetics [64]. Metabolic abnormalities of bone in patients with diabetes may be the direct consequence of insulin deficiency or insulin resistance and hyperglycemia on the bone and its metabolic milieu. The effects may also be due to advanced glycation end products (AGEs), adipokines, abnormal cytokine production and their deleterious effects on bone cells and neuromuscular/skeletal interactions[64].

Iowa Women's Health Study had showed that women with type 1 diabetes mellitus were at risk of hip fractures than without T1DM [65].In the same way women with T2DM are at more risk of developing fractures than without it. Longer duration T2DM predisposes to frequent falls probably because of associated peripheral neuropathy, thus increasing the probability of having fractures despite having better BMD[64].It is prudent to provide appropriate clinical intervention to skeletal disease in order to achieve an optimal bone health in these patients.

Possible mechanisms and risk factors for osteoporosis in T1DM:

The presence of micro and macrovascular complications for a prolonged period with poor glycemic control rather than duration of disease per se predisposes to lower BMD in T1DM.The complications include retinopathy, nephropathy, peripheral neuropathy, and peripheral vascular disease. Both retinopathy and peripheral neuropathy leads to hampering of physical activity and neuromuscular/ skeletal interactions,

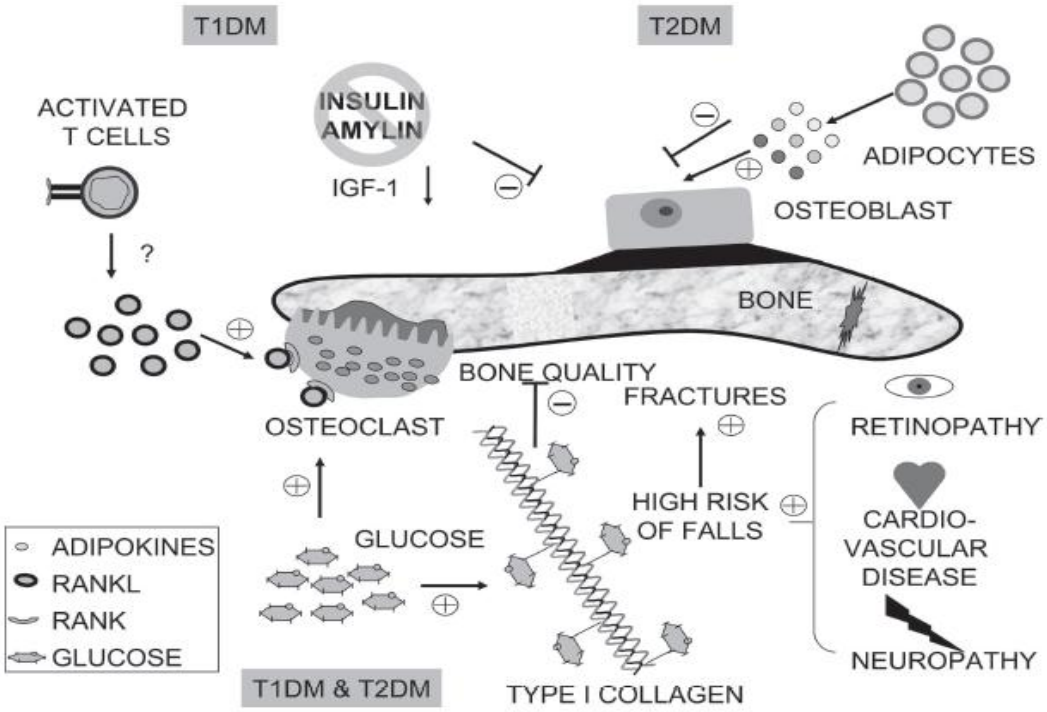
and enhanced susceptibility to fall causing lowering of BMD[65].One study had proved that patients with retinopathy has 72% chance of having lower BMD. Both peripheral neuropathy and nephropathy has been linked to poor bone mineral density[65].

Possible mechanisms behind these changes in T1DM are insulinopenia and the anabolic effects of insulin on bone is lost, also the co-existing amylin deficiency also contributes to lower BMD because of increased osteoclast mediated bone resorption[65].

Possible mechanisms and risk factors for osteoporosis in T2DM:

The discrepancy between the onset of the disease and the diagnosis of T2DM is a very important factor in determining its major complications such as metabolic bone disease. There is usually a time lag of at least 5-10 years between the onset and diagnosis of diabetes. The Rotterdam study, so far the largest study on BMD in diabetics had showed treated diabetic patients are at increased risk of fractures in spite of having better BMD[65].

In contrary to T1DM with absolute insulin and amylin deficiency, T2DM is associated with resistance to insulin action peripherally there will be an impaired secretion of insulin following a metabolic challenge with glucose. Hyperglycemia is a potential detrimental factor affecting bone homeostasis.



Effects of diabetes on metabolic milieu of bone.

Uncontrolled hyperglycemia is the major contributing factor for all the pathophysiological consequences in patients with diabetes. The intricate relationships between hyperglycemia and BMD have not been studied in detail. The osteoclast derives its nutrition mainly from glucose and it has a robust machinery to dose-dependently modify its function in vitro. Hyperglycemia may impair bone quality by non enzymatic glycosylation of type I collagen and various bone proteins.

Other possible deleterious effects on bone homeostasis by uncontrolled hyperglycemia includes increased urinary calcium excretion which is secondarily due to elevated renal threshold to glucose excretion

and possible interplay between elevated blood glucose concentrations and PTH/vitamin D system. A study in small healthy cohorts had showed hypercalciuria and hypocalcemia which was associated with diminished levels of parathyroid hormone after challenge with oral glucose load[65]. A study in hospitalized patients with T2DM proved that return of the euglycemic status resulted in normalization of urinary calcium and phosphate excretion, serum vitamin D levels and the elevated serum phosphate levels, but without undue responses in PTH levels or serum calcium.

A prevalence study from New Zealanders revealed lower serum25-Hydroxyvitamin D3 levels in subjects with newly detectedT2DM and in patients with impaired glucose tolerance. In a prospective study from Dutch people 39% of people with T2DM,associated with vitamin D deficiency. However with regards to controversy surrounding obesity in diabetes, possibly the adverse effects of hyperglycemia on the bone homeostasis are heavily counterbalanced by the beneficial effects of obesity on bone mineral density, a theory now strongly being challenged. The role of adipokines on human disease had been studied in great detail.Leptin the best-studied adipokine so far with regard to its effects on bone was briefly discussed earlier. Recently, adiponectin and resistin have been shown to execute its protective effects of obesity on the skeleton .Two principal pathways that were proposed to influence the skeletal effects of leptin are central and peripheral. Both these paths have

opposite effects. The predominant central effect on the skeleton isby restraining osteoblast proliferation there by leading to suppression of bone formation. The central effects are mediated through sympathetic pathway. The central pathway is the major way by which it mediates its action. The receptors for adiponectin are expressed on both osteoblastic and osteoclasticcell lineages and osteon synthesis in cultured osteoprogenitor cells is suppressed by adiponectin. This suppression was blunted in the presence of insulin.

Resistin too is produced by both osteoblastic and osteoclastic cell lineages. Resistin stimulates the osteoclast development and has no effect on osteoblastic differentiation. Together the adipokines have both positive as well as negative effects on bone homeostasis that do not fully account for an better bone mineral density values in obese people. Adiponectin levels are depressed in both obese and diabetic people and it antagonizes the inflammatory mediators there by offering protection to endothelial and vascular smooth muscle cells, and has beneficial effects on ventricular remodeling. These adipokines in over all have a net beneficial effect on osseous microenvironment in patients with T2DM, However their unwarranted effects on the cardiovascular system make the patients with T2DM susceptible to falls, which makes them fracture prone that has been related to osteoporosis despite higher BMD.

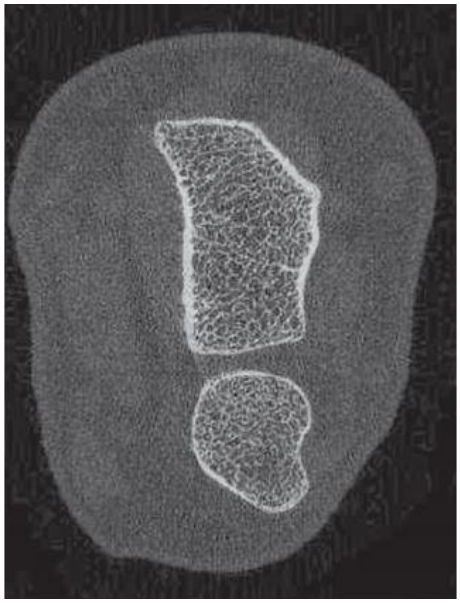
Clinical recommendations based on evidence based medicine:

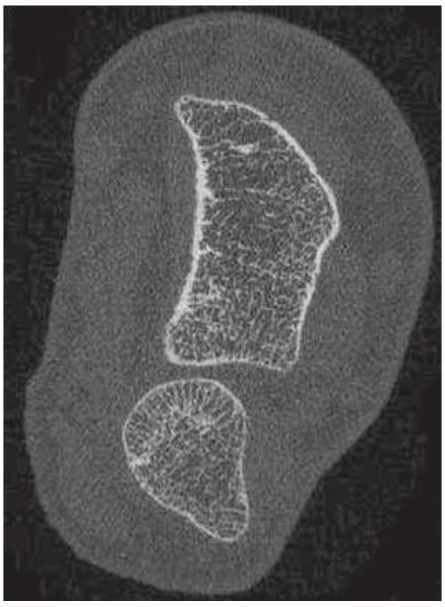
Most of the current osteoporosis therapeutic intervention trials Involve the diabetic population. There no consensus based guidelines currently. Exist to direct the interventional models in the management of diabetic osteoporosis. Any patient with T2DM represents a prognostic and diagnostic perplexity because the importance of measuring BMD to assess the osteoporotic fracture risk is constrained by two main factors:

1) Defective quality of bone.
2) Increased susceptibility to falls.

Maintenance of euglycemic status is essential to curtail the degree of non-enzymatic glycosylation of type 1collagen in the bone. Vascular complications are delayed by maintaining adequate glycemic control. It is essential to have a check on the risk factors for the falls and consideration should be given to the neurological and cardiovascular status in addition to assessing the balance.

A recent meta-analysis has advocated proper implementation of systematic exercise program to improvise the muscle strength, improve the balance, and proprioception, visual health with attention to cataracts, use of hip braces to decrease the risk of falls and fractures[67]. Calcitriol and oral calcium supplementation had shown encouraging out comes in a small cohort of nondiabetic women with attendant reduction in fracture rate by almost 50%. It still remains elusive whether this can also be extrapolated to diabetic people.





NORMAL BONE IN HRCT **OSTEOPOROTIC BONE IN HRCT**

Methods to assess Bone Mineral Density:

Currently there are various methods available to qualitatively assess the mineral contents of the bone. All of them are noninvasive with low radiation hazard.

These tests include:

1) Dual-energy X-ray absorptiometry (DXA or DEXA)
2) Quantitative computed tomography (QCT)
3) Qualitative ultrasound (QUS)
4) Single photon absorptiometry (SPA)
5) Dual photon absorptiometry (DPA)
6) Digital X-ray radiogrammetry (DXR)
7) Single energy X-ray absorptiometry (SEXA)

Though ultrasound had proved cost effective, DEXA still remains the most commonly used. It is a sensitive assay to assess the bone mineral density.

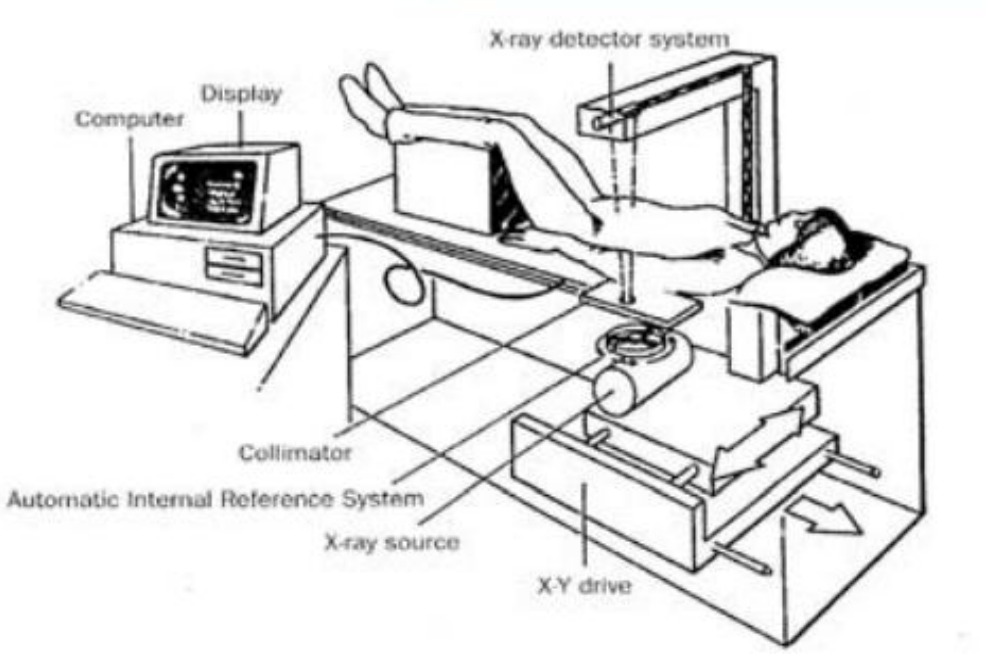
DUAL ENERGY X RAY ABSORPTIOMETRY:

Dual-energy X-ray absorptiometry is the best technique that is currently available to measure bone density (BMD). The physics behind the genesis of dual energy X ray is that, X rays are generated in Coolidge tube by tiny negatively charged particles called electrons which exists from a wire filament when heated. These electrons are accelerated by high voltage towards metal target made of tungsten. In the target some of the electron kinetic energy is converted into X- ray energy. When X ray particles are passed through the human body there is attenuation in the intensity of the beam. Now to measure the BMD, X ray beam is passed through the bone and the attenuation is measured and expressed in gram/cm2 which accounts for mineral density of bone. Likewise in dual energy X ray absorptiometry, attenuation is measured between high and low energies. Previously used in this technology are radioactive gadolinium 153 because of potential hazards associated with its use the photons are replaced by X ray tube [70]. Typically this technique involves scintillation detector mounted on C arm. The purpose of this arrangement is to expose the patient in a pencil beam of x rays in a rectilinear fashion.

DEXA SCANNER

Measurements of the variables from the DEXA scan:

The values are scored by T- score and Z- score. Each of this score ranges from negativity to positivity. A Negative score indicates decreased BMD and a Positive score indicating higher. In addition it measures fat content in grams, lean mass, regional fat content and bone mineral content.



PARTS OF DEXA SCANNER

Importance of T- score:

For the measure of osteoporosis the relevant variable is **T score**. A T score may show how much a bone mass may deviate from the average bone mass of a healthy adult. It refers to the bone mineral density of that particular site compared with young normal reference mean population. In simplistic terms it is the comparison of bone mineral density of patients with that of a normal 30 year old of same sex and ethnicity. This value is compared with that of postmenopausal women and men over fifty years of age to evaluate the risk of osteoporosis[71]. One standard deviation refers to 10-20% difference in bone mass. For example if the patient's bone is less dense its SD -2 or -3 indicating the patient's bone is 20 to 30% less dense than average 30 year old.

WHO CRITERIA FOR OSTEOPOROSIS:

T- SCORE	DIAGNOSIS
> - 1.O	ADEQUATE BMD
-1.O TO -2.5	OSTEOPENIA
< - 2.5	OSTEOPOROSIS
< - 2.5 with fractures	SEVERE OSTEOPOROSIS

WHO- WORLD HEALTH ORGANIZATION

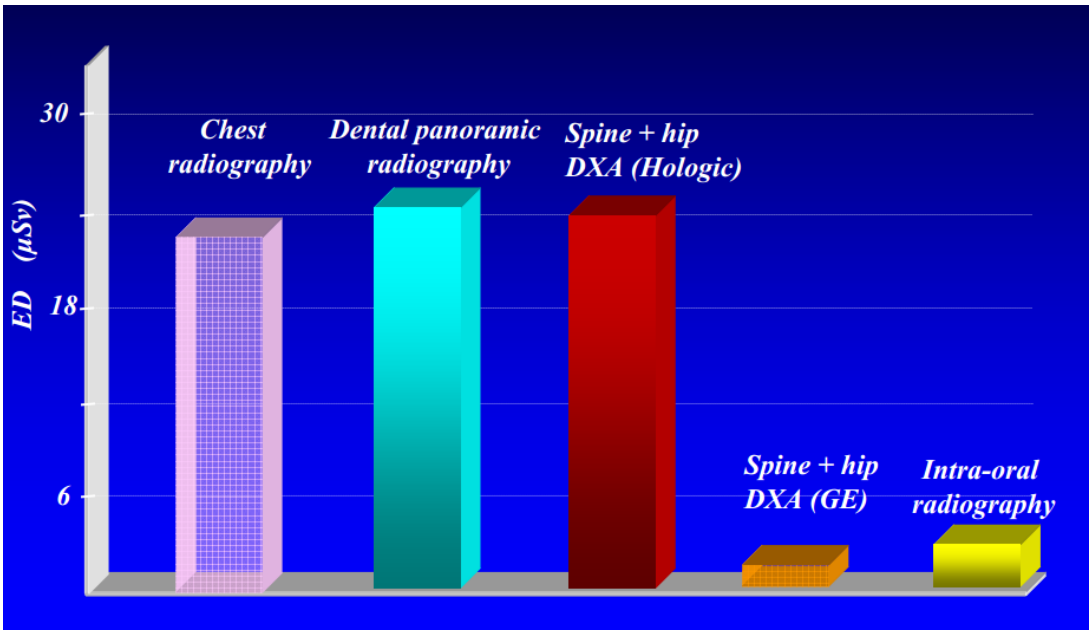
Importance of Z score:

A **Z-score** compares the patient's bone density to the average for same age and gender. For example a 60 year female patients BMD is compared with that of average BMD of 60 year old females. In simplistic terms it is comparison of age matched normal. It refers to the number of times in standard deviation in which patients BMD differs from that of their age, sex and ethnicity. For evaluation of osteoporosis T score is considered more significant than Z score.

Z score	**Diagnosis**
> - 1.5	ADEQUATE BMD
-1.5 TO -2.5	OSTEOPENIA
< - 2.5	OSTEOPOROSIS

Radiation dose in DEXA imaging:

Albabese et al had compared various modalities of radiological investigations and the radiation dose associated with it. It has been found that the average DEXA scanner exposes the patient to radiation dose of 0.3 micro Sievert units this is hardly any radiation dosage when compared with chest X ray, which carries a radiation dosage of 50 micro Sievert units. Similarly Njeh et al had proved the radiation dose was negligible when compared with environmental exposure.



Comparison of available radiological investigation's in respect to their radiation dosage**. NOTE**; New generation pencil beam DEXA has an exposure rate of 0.3- 0.4 micro Sieverts.

Relationship between obesity, osteoporosis and diabetes mellitus- Unifying the topics:

Obesity and diabetes mellitus are a part of metabolic syndrome. It has been observed from various studies that majority of patients with diabetes mellitus suffer from obesity on the contrary, only less than 10% of patients with obesity suffer from diabetes mellitus[64] .To favor this fact majority of osteoporotic treatment studies involves obese diabetics [64,65].

Emerging observations from western literature have implicating that diabetes mellitus is no more protective against the development of osteoporosis [64].To some extent osteoporosis is even called as obesity of bone [68].

The number of diabetic population in India had already reached 60 million it's the right time to concentrate on the much underappreciated complications of diabetes like osteoporosis in addition to micro and macro vascular complications which have been addressed extensively.

It's not elusive what is contributing to decreased BMD in diabetes either the adiposity associated with T2DM is the major contributing factor via leptin pathway or diabetes per se is contributing to pathogenesis via it's collagen cross linking pathway. With diabetes providing a substrate for obesity and obesity proving a substrate for osteoporosis, these three disorders are inter mingled and a holistic approach is needed to address these three complicated issues.

Hypothesis generation:

With recent advances in modern science and the increase in life expectancy places osteoporosis as one of the major health public problems to be addressed in the India. There are studies which have showed conflicting results, with diabetes is protective against the development of osteoporosis [69]. But subsequent studies had not proved so. If at all low BMD is a complication of diabetes, whether obesity is the major risk factor for the development of low BMD or it's a complication of diabetes per se is to be ascertained. If there is any additional contributing factors like levels of vitamin D influencing the disease outcome will also be ascertained.

With this study aimed at the assessment of BMD in obese and non-obese diabetics the pattern of prevailing bone mineral density in this subset of population (South East Asians) can be assessed.

MATERIALS AND METHODS

This is a single center cross sectional study, done at Government Royapettah Hospital, Diabetology department. This study protocol was approved by the Ethical committee for research studies of Government Kilpauk Medical College Hospital, Chennai.

INCLUSION CRITERIA:

Patients admitted in the general ward of Government Royapettah Hospital for diabetic control and patients attending Diabetology department on outpatient basis are included in the study. Patients with T2DM were included in the study. Age group included in the study was less than 50 years. The study period is between July 2012-December2012.The patients recruited to this study were diagnosed to have diabetes using the American diabetes association criteria. Detailed clinical profile was noted, for each patient. Patients with written informed consent about the procedure were subjected to DEXA imaging for the evaluation of osteoporosis.

EXCLUSION CRITERIA:

1. Age more than 50 years.
2. Smoker.
3. CKD.

4. Patients on calcium and Vitamin D supplementations.

5. Patients with drugs affecting calcium metabolism.

6. Patients taking pioglitazone for diabetes.

7. Female patients who had attained menopause were excluded from the study.

8. Patients with peripheral neuropathy and cataracts.

9. Patients with proven underlying malignancy.

Statistical analysis was done to identify significance and correlation between bone mineral density and obesity. Statistical analysis was done using SSPS 15 software. Univariate analysis was done with paired t test and Pearson product moment correlation coefficient.

A Total of 50 patients, all of them fulfilled the ADA criteria for diabetes were subjected to DEXA imaging. All the patients included in the study were type 2 diabetes mellitus. Out of 50 patients included in the study 25 patients were obese, fulfilling the WHO criteria for obesity. Body mass index of more than 30 were included in the test group. Patients with normal body mass index, fulfilling WHO criteria with a BMI of less than 24.99 were included in the control group. The control group consists of 25 patients. The sex ratio being approximately equal in both test and control group. Hence forth sex as a confounding variable had been removed if it had been present.

OBSERVATIONS AND RESULTS

TABLE-1:

SEX COMPOSITION OF STUDY POPULATION.

SEX	OBESE	NONOBESE
MALE	13	12
FEMALE	12	13

TOTAL NUMBER OF OBESE DIABETICS= 25

TOTAL NUMBER OF NON OBESE DIABETICS= 25

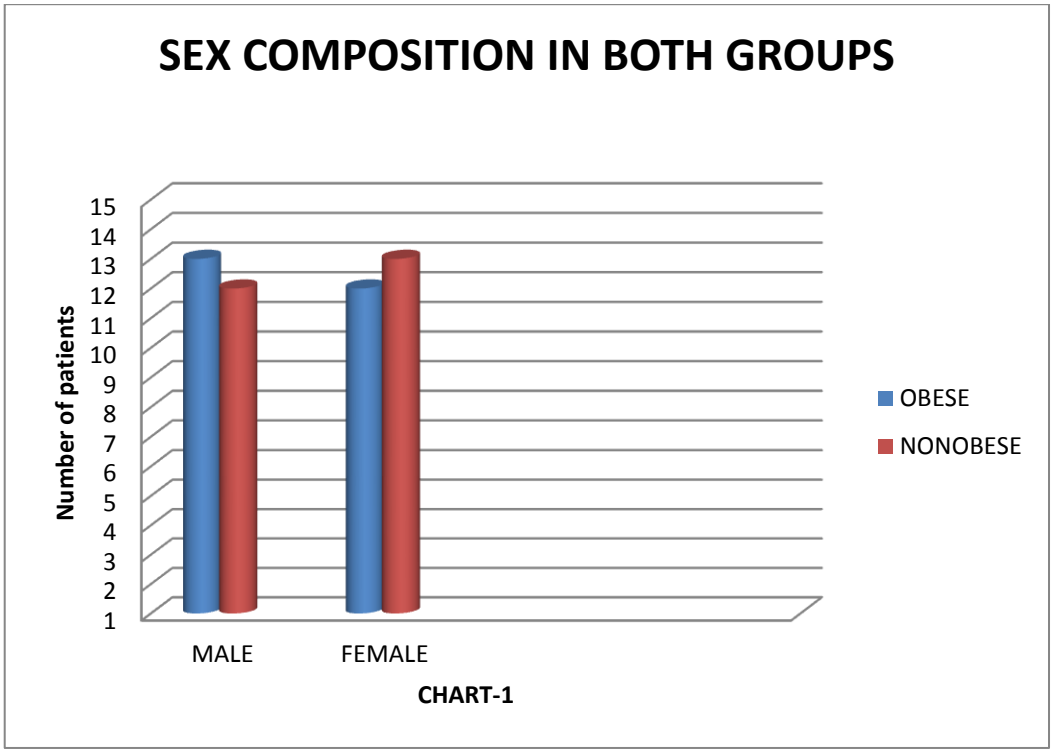


CHART-1

TABLE 2:

SEX COMPOSITION AND COMPARISON WITH IN THE GROUP AND BETWEEN GROUPS.

			SEX		
			Male	**Female**	**Total**
Group	Obese	Count	13	12	25
		% within Group	52.0%	48.0%	100.0%
	Non_obese	Count	12	13	25
		% within Group	48.0%	52.0%	100.0%
Total		Count	25	25	50
		% within Group	50.0%	50.0%	100.0%

P=1.000[NS]- sex composition statistically not significant.

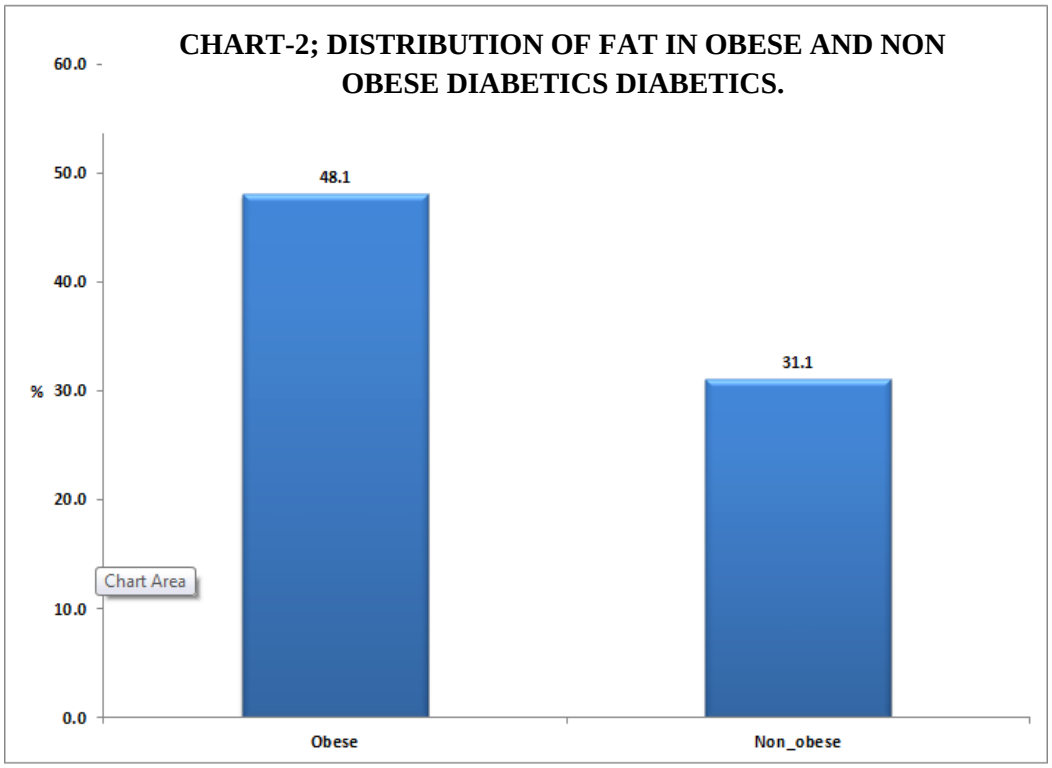
Variables measured in the study:

The important variables that were measured while subjecting the patient to DEXA imaging – lunar prodigy 2nd generation scanner that uses pencil beam for the evaluation of BMD are total fat percent of the body, type and distribution of fat content - that is android and gynoid obesity, lean mass and the important variable that negates the net weight bearing

effect on the bone, the percent fat mass. The T and Z scores of lumbar spines were taken as standard for the assessment of BMD.

The percent fat mass is calculated from the two known variable from the data obtained from DEXA imaging. It is the ratio between the fat mass to body weight.

$$\text{PERCENT FAT MASS} = \frac{\text{FAT MASS [GRAMS]}}{\text{TOTAL BODY WEIGHT [GRAMS]}}$$



The above observation shows the average fat percentage in obese group was 48.1% and in non- obese group was 31.1%

TABLE -3

VARIABLES MEASURED

Group		Age	Weight	Height	BMI	Fat per	Duration
Obese	Mean	41.336	85.824	159.36	33.577	48.076	10.840
	N	25	25	25	25	25	25
	Std. Deviation	5.3582	14.2375	7.697	4.9652	4.4549	3.3126
	Minimum	28.5	60.0	140	24.6	39.0	3.0
	Maximum	50.0	125.9	172	52.4	57.0	16.0
Non-obese	Mean	42.000	60.400	163.04	22.482	31.112	11.520
	N	25	25	25	25	25	25
	Std. Deviation	4.3493	6.3836	6.387	1.3779	6.1758	3.2031
	Minimum	34.0	50.0	149	19.4	23.6	7.0
	Maximum	48.0	70.0	174	24.5	44.4	18.0
Total	Mean	41.668	73.112	161.20	28.029	39.594	11.180
	N	50	50	50	50	50	50
	Std. Deviation	4.8415	16.8563	7.242	6.6638	10.0903	3.2431
	Minimum	28.5	50.0	140	19.4	23.6	3.0
	Maximum	50.0	125.9	174	52.4	57.0	18.0

In addition, the study and control population were subjected to vitamin D analysis using CLIA method.

From the measured variables the mean BMI in obese diabetics was 33.577 and in non-obese it was 22.482. The mean fat distribution in obese group was 48.076% where as that of non-obese group was 31.112%. The proportion of android and gynoid fat distribution is almost similar in obese diabetic group with android distribution being 51% and gynoid type was 48.2%.

The mean Bone Mineral Density in obese diabetics was 1.0856 g/cm2, where as that of non-obese group was 1.32232. The average vitamin D levels observed in this study in obese diabetics was 23.059 ng/dl and in non-obese patients was 27.596 ng/dl. The mean Percent Fat Mass [PFM] in obese diabetics was 0.417 and in non-obese group it was 0.2688.

TABLE-4

VARIABLES MEASURED CONTINUED.

Group		VIT_D	ANDROID FAT	GYNOID FAT	BMD	PFM
Obese	Mean	23.059	51.000	48.219	1.08536	.41728
	N	25	25	25	25	25
	Std. Deviation	3.8362	6.2066	5.2614	.137835	.085892
	Minimum	19.6	39.7	38.3	.879	.256
	Maximum	34.6	65.4	59.2	1.324	.561
Non-obese	Mean	27.596	33.672	28.320	1.32232	.26880
	N	25	25	25	25	25
	Std. Deviation	6.2004	6.5839	6.0570	.131812	.041467
	Minimum	19.0	3.6	18.5	1.067	.198
	Maximum	46.0	39.4	38.6	1.497	.342
Total	Mean	25.328	42.336	38.270	1.20384	.34304
	N	50	50	50	50	50
	Std. Deviation	5.5937	10.8026	11.5127	.179274	.100398
	Minimum	19.0	3.6	18.5	.879	.198
	Maximum	46.0	65.4	59.2	1.497	.561

TABLE-5

ABNORMAL BMD IN OBESE AND NONOBESE DIABETICS COMPARED

TYPE	OSTEOPENIA	OSTEOPOROSIS	TOTAL
OBESE DIABETIC	16	4	25
NON OBESE DIABETIC	3	-	25

Total number of patients with osteopenia in both groups were 19 [total number=50] and total number of patients with osteoporosis were 4[total number = 50]

In total 38% of the diabetics had osteopenia whereas only 8% of the total diabetic population including both obese diabetic and non-obese diabetics exhibited osteoporosis.

So from the above observation it is clear that osteopenia may be the most prevailing type of abnormal BMD in obese diabetic population.

TABLE-6

COMPARITIVE PREVALENCE OF OSTEOPENIA IN OBESE AND NON OBESE DIABETICS

			OSTEOPENIA		
			Yes	**No**	**Total**
Group	Obese	Count	16	9	25
		% within Group	64.0%	36.0%	100.0%
	Non-obese	Count	3	22	25
		% within Group	12.0%	88.0%	100.0%
Total		Count	19	31	50
		% within Group	38.0%	62.0%	100.0%

P=0.000

The prevalence of osteopenia in obese diabetics were 64% P < 0.05[significant]

TABLE-7

COMPARITIVE PREVALENCE OF OSTEOPOROSIS IN OBESE AND NON OBESE DIABETICS

			OSTEOPOROSIS		
			Yes	**No**	**Total**
Group	Obese	Count	4	21	25
		% within Group	16.0%	84.0%	100.0%
	Non-obese	Count	0	25	25
		% within Group	.0%	100.0%	100.0%
Total		Count	4	46	50
		% within Group	8.0%	92.0%	100.0%

P=0.110

The prevalence of osteoporosis alone in obese diabetics was 16%. P = 0.110 [not significant]

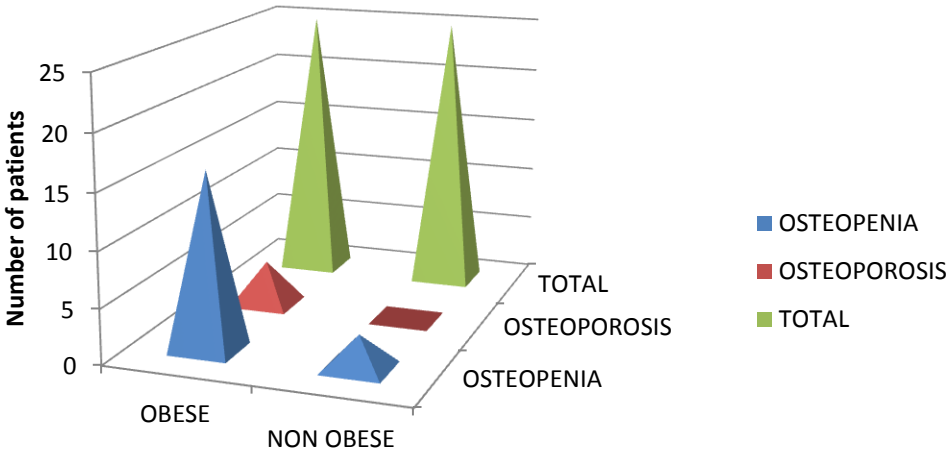


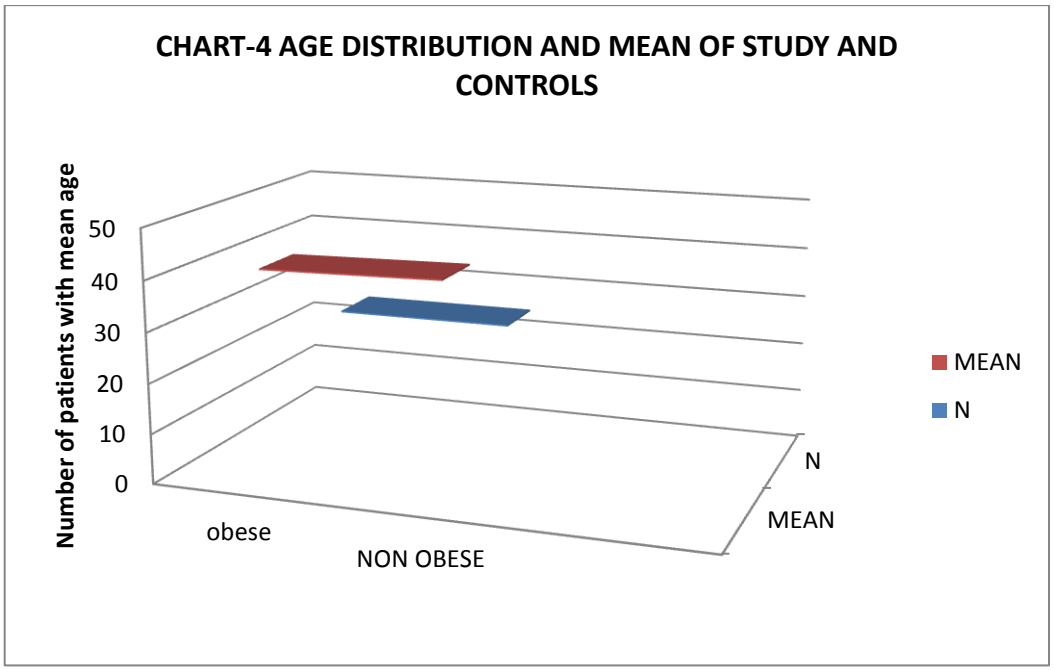
CHART-3 SHOWING NUMBER OF PATIENT WITH OSTEOPENIA AND OSTEOPOROSIS IN BOTH GROUPS

As noted from the above observation out of 25 patients in obese diabetic group 20 of them had abnormal bone mineral density. Out of 20 patients 16 of them were osteopenic and only 4 of the patients were osteoporotic. This observations is statistically significant [P = < 0.000].whereas in the control group that consists of non-obese diabetics the total number of patients with abnormal BMD is only three. All three of them were osteopenic and none exhibited the pattern of osteoporosis. The above observation was not statistically significant [P=0.110].

TABLE-8

T-TESTSHOWING NO STATISTICAL CORRELATION IN DURATION

	Group	N	Mean	Std. Deviation	P-value
AGE	Obese	25	41.336	5.3582	0.633
	Non-obese	25	42.000	4.3493	
DURATION	Obese	25	10.840	3.3126	0.464
	Non-obese	25	11.520	3.2031	



From the above observations the age clustering was early 40's in both the sex for both obese and non-obese diabetics. When tests of significance were performed for both age and duration influencing the outcome of the study, there was no statistical significance of either.

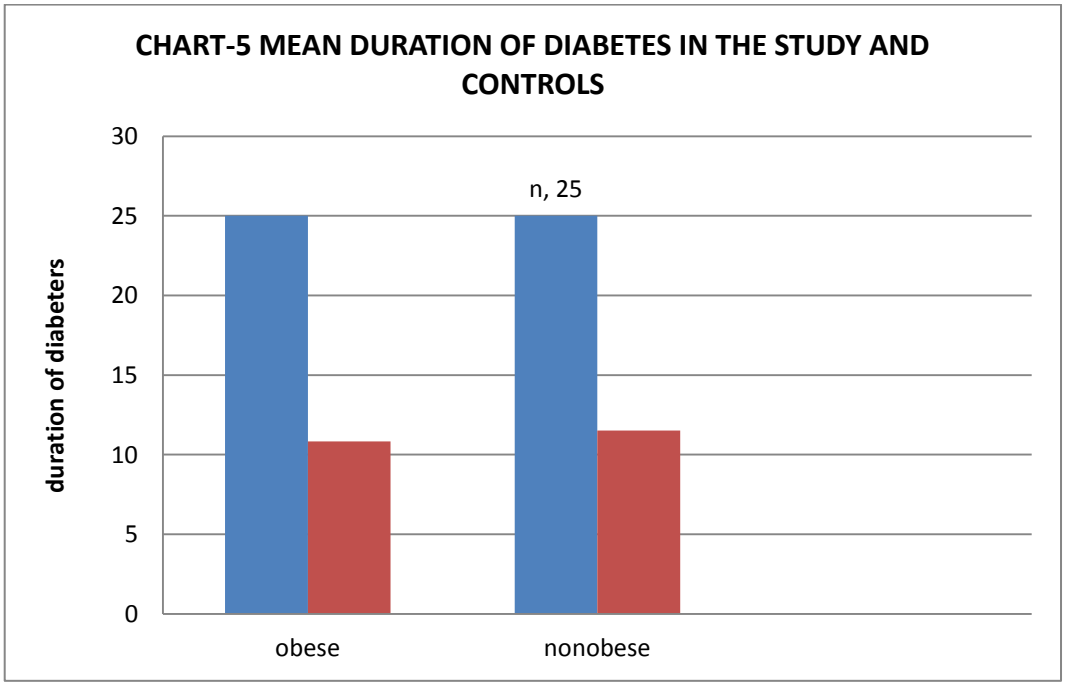
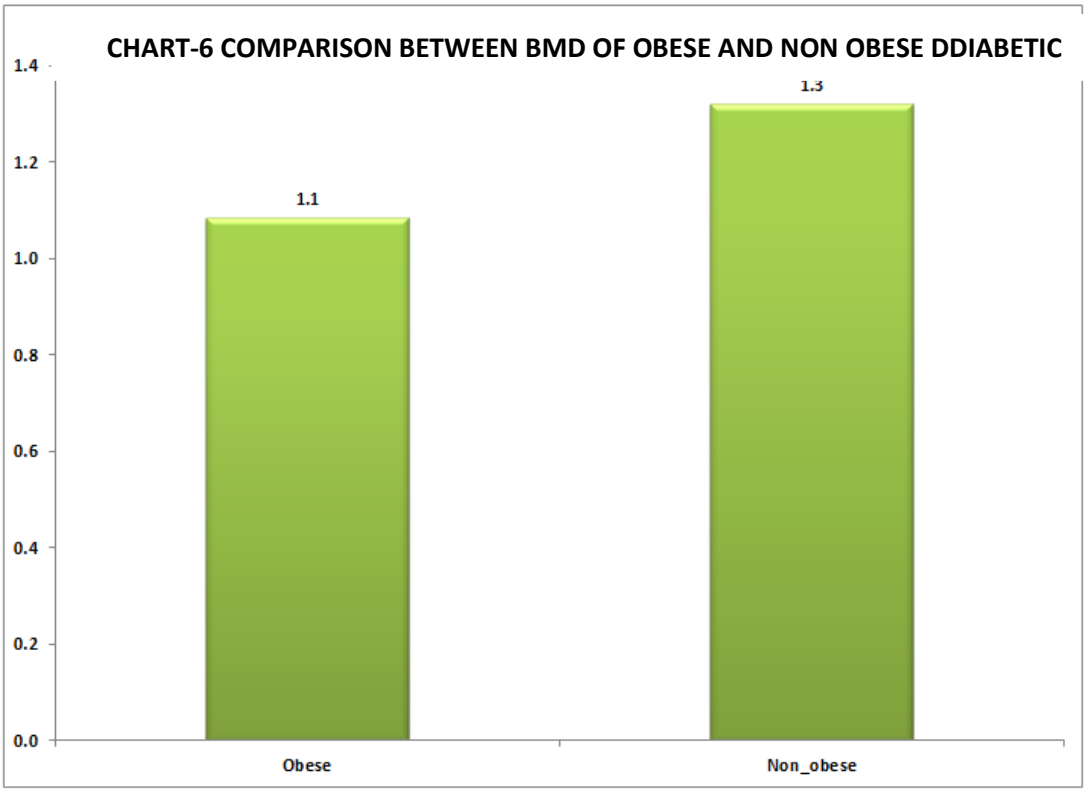


TABLE-9

SHOWING STATISTICAL CORRELATION BETWEEN T AND Z SCORE WITH REFERENCE TO BMD

	Group	N	Mean	Std. Deviation	P-value
T SCORE	Obese	25	-1.360	1.2066	0.000
	Non-obese	25	1.648	1.4057	
Z SCORE	Obese	25	-1.200	1.0642	0.000
	Non-obese	25	1.124	1.2166	
BMD	Obese	25	1.08536	.137835	0.000
	Non-obese	25	1.32232	.131812	



The above observation shows the comparison between T and Z scores and the bone mineral density in obese and non -obese diabetics. The average T score in obese diabetic was – 1.360 which is in the osteopenic range [A score of -1 to -2.5 indicates osteopenia]. The average Z score being -1.20 in obese diabetic.

For both the variables compared with BMD the P value was statistically significant [P = 0.000].

The average BMD in obese diabetics were 1.08536 when compared to non -obese diabetics were 1.32232 which is statistically significant [P = 0.000].

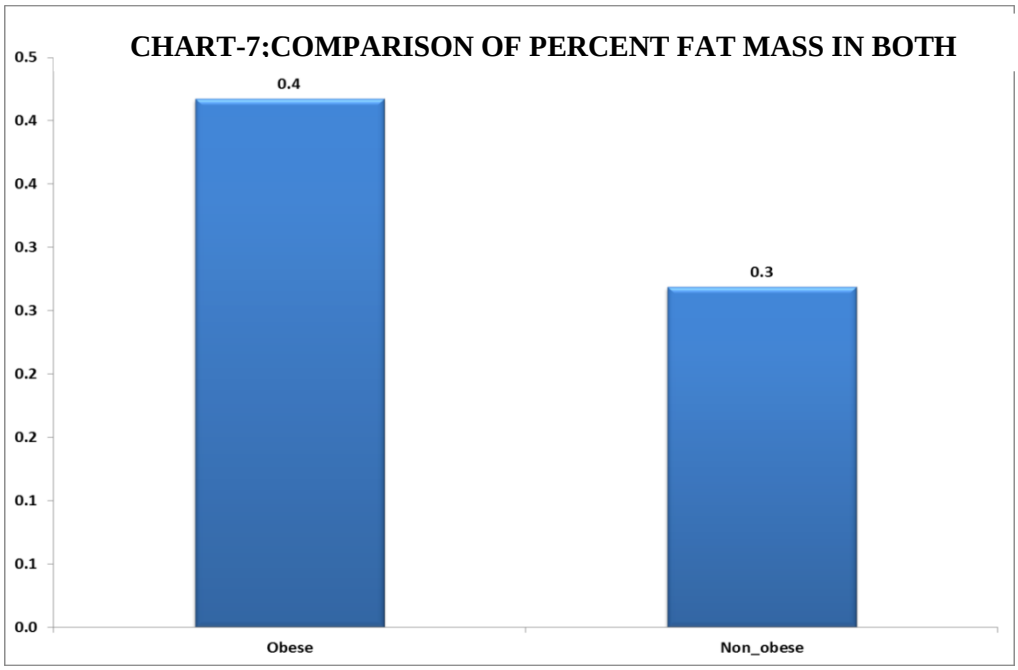
TABLE-10

T TEST AND GROUP STATISTICS BETWEEN VARIABLES

MEASURED BY DEXA

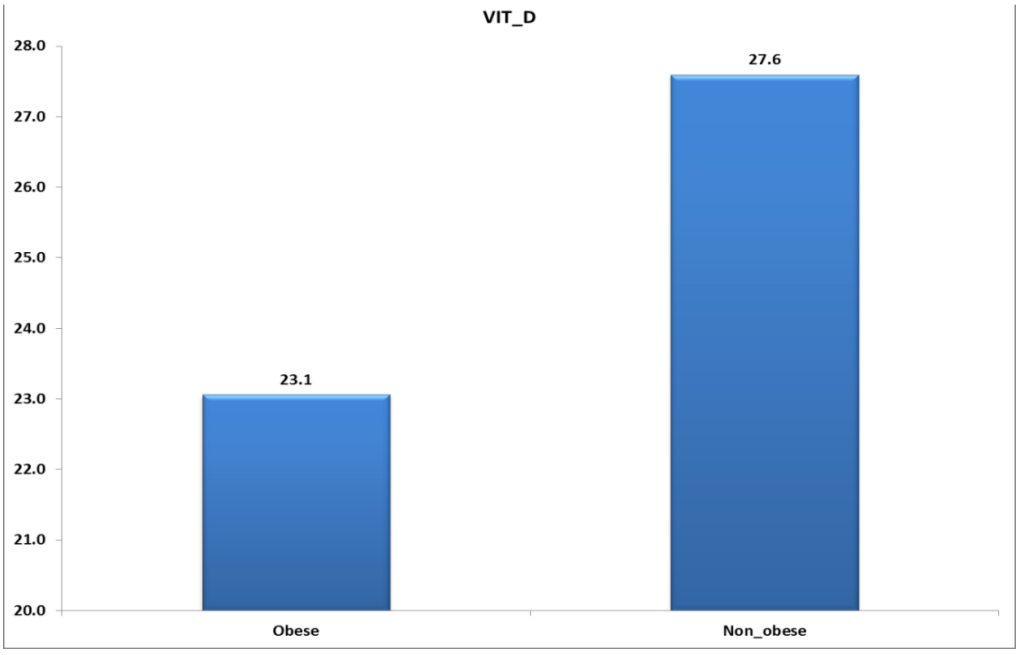
	Group	N	Mean	Std. Deviation	P-value
BMI	Obese	25	33.577	4.9652	0.000
	Non-obese	25	22.482	1.3779	
FAT PER	Obese	25	48.076	4.4549	0.000
	Non-obese	25	31.112	6.1758	
VIT_D	Obese	25	23.059	3.8362	0.003
	Non-obese	25	27.596	6.2004	
ANDROID FAT	Obese	25	51.000	6.2066	0.000
	Non-obese	25	33.672	6.5839	
GYNNOID FAT	Obese	25	48.219	5.2614	0.000
	Non-obese	25	28.320	6.0570	
BMD	Obese	25	1.08536	.137835	0.000
	Non-obese	25	1.32232	.131812	
PFM	Obese	25	.41728	.085892	0.000
	Non-obese	25	.26880	.041467	

CHART-7:COMPARISON OF PERCENT FAT MASS IN BOTH

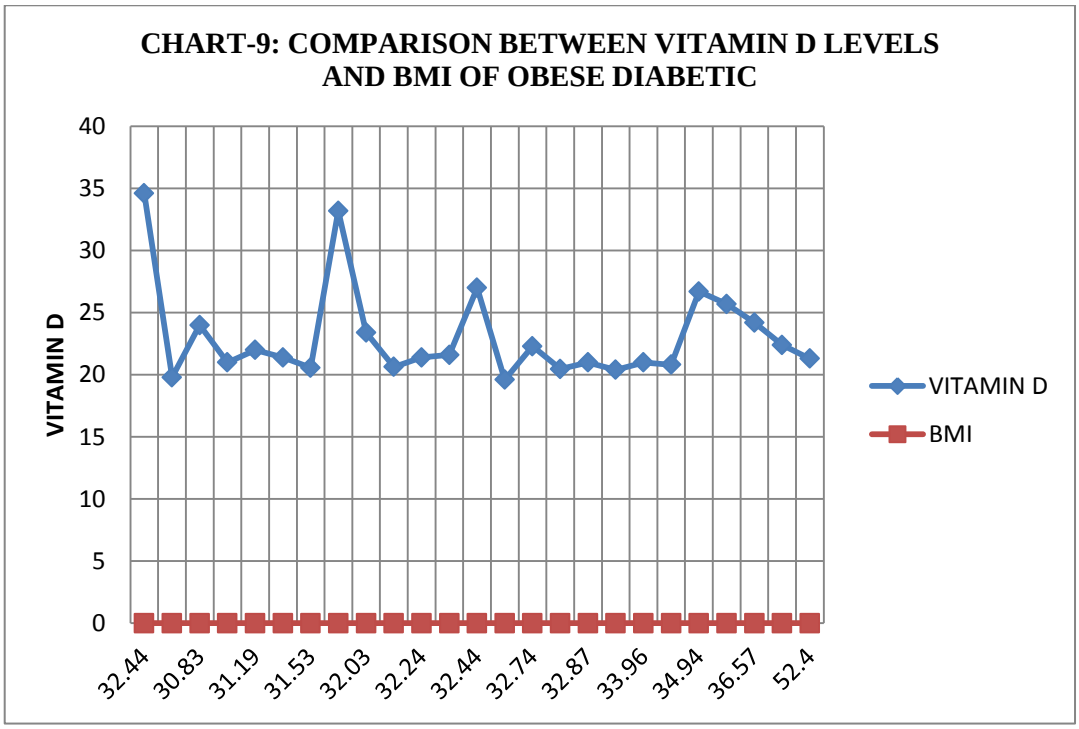


The average percent fat mass [PFM IN X AXIS] in obese diabetics were 0.417 and in non- obese group were 0.28

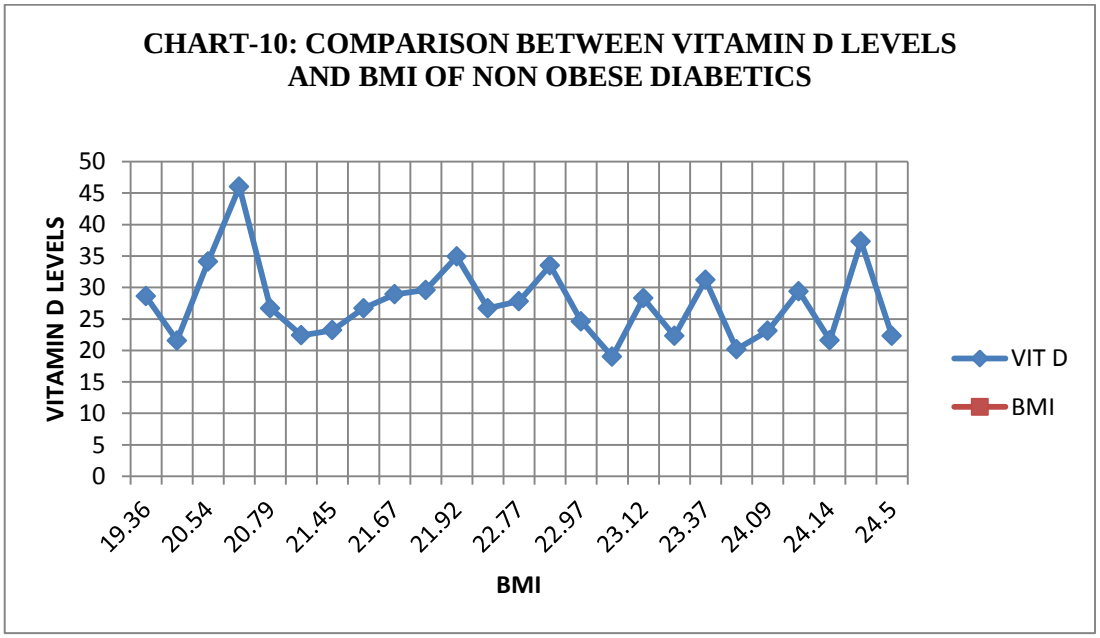
CHART-8: COMPARISON OF VITAMIN D LEVELS IN BOTH GROUPS



The average vitamin D levels[X -AXIS] in obese group were 23.1 ngml and in non obese were 27.6 ng/ml



The mean value of vitamin D levels falls between the range of 20 to 25 ng/ml in obese diabetics.



The mean value of vitamin D levels falls between the range of 25 to 35 ng/ml in non-obese diabetics.

The above observation regarding the comparison of vitamin D levels with reference to BMI in obese and non -obese diabetics indicates both the groups were vitamin D insufficient. The average vitamin D levels in obese diabetics were23.059 ng/ml,where as that of non-obese diabetics was slightly on the higher side with a mean value of 27.59 ng/ml. But as per the international levels both groups were vitamin D insufficient if not deficient. The P value in group statistics is significant [P = 0.003], but within the obese diabetics the correlation between BMI and vitamin D levels were not statistically significant.

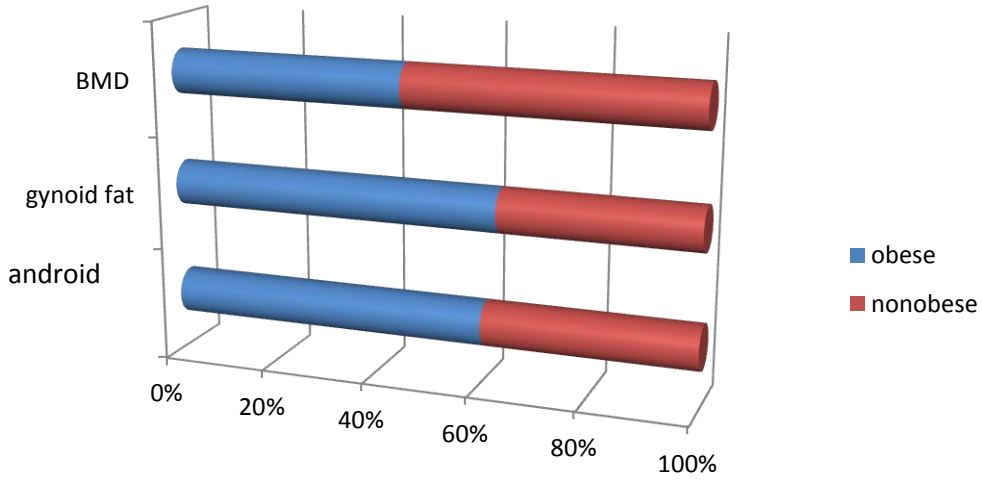


CHART-11: DISTRIBUTION OF ANDROID AND GYNOID FAT IN OBESE AND NON OBESE DIABETICS WITH REFERENCE TO BMD

The above observation shows the distribution of android and gynoid fat in obese and non -obese diabetics. There is a statistical correlation between pattern of obesity and the mean BMD. The mean android fat mass was 51.0 % and mean gynoid mass was 48.219% in obese diabetics and BMD of obese people was 1.085 g/cm^2 . Meanwhile

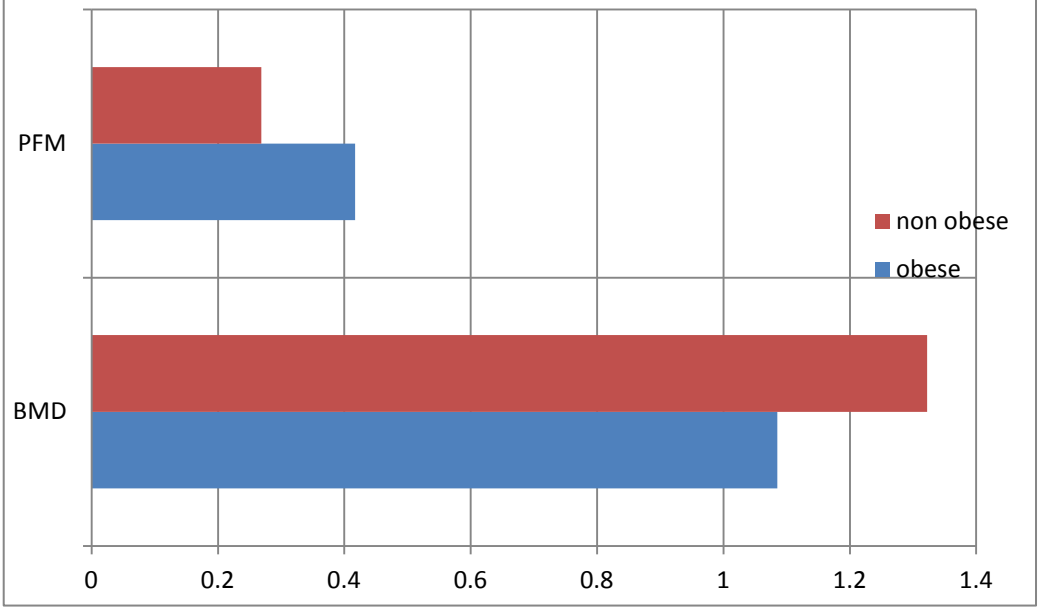
the mean android fat mass in non-obese diabetic was 33.672% and gynoid fat mass was 28.32% and BMD of non-obese patients was 1.32232. The correlation between the type of fat mass and BMD was statistically significant with both android and gynoid obesity associated with decreased BMD[P = 0.000].

TABLE-11

COMPARISON OF BMD WITH PFM SHOWS STATISTICAL SIGNIFICANCE

Group	N	Mean	STANDARD DEVIATION	P Value
BMD OBESE	25	1.085	0.138735	0.000
NON OBESE	25	1.32232	0.131812	
PFMOBESE	25	0.41728	.085892	0.000
NON OBESE	25	0.26880	.041467	

Chart-12: COMPARISON OF PFM AND BMD IN OBESE AND NON OBESE DIABETICS



From the above observation it is obvious that when the percent fat mass is more, there is a decrease in BMD. The mean fat mass in obese diabetic is 0.417 and the mean BMD in obese diabetic was 1.085 g/cm2. Whereas the mean fat mass for a non- obese diabetic was 0.26880 and mean BMD for non- obese diabetic was 1.32232. The observation was statistically very significant [P = 0.000].

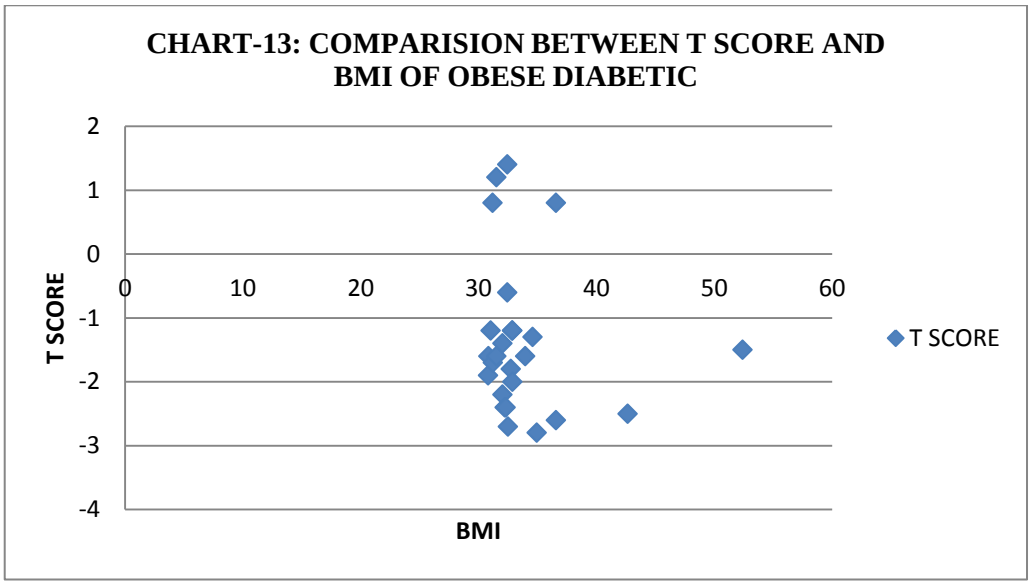
TABLE-12

PEARSONS CORRELATION BETWEEN VARIABLES

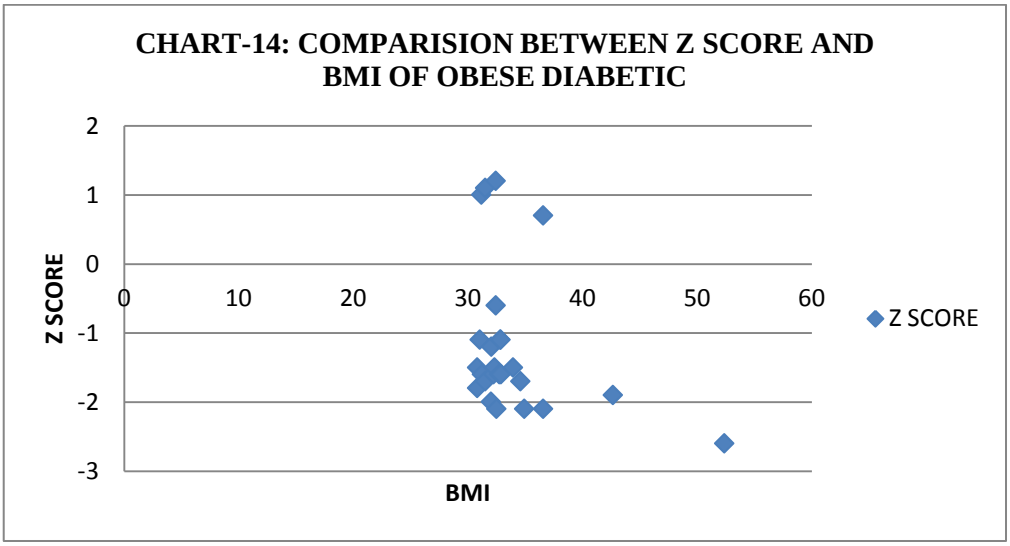
		BMI	T SCORE	Z SCORE	VIT_D	DURATION
BMI	Pearson Correlation	1	-.701**	-.714**	-.426**	.063
	Sig. (2-tailed)		.000	.000	.002	.665
	N	50	50	50	50	50
T SCORE	Pearson Correlation	-.701**	1	.977**	.529**	-.096
	Sig. (2-tailed)	.000		.000	.000	.505
	N	50	50	50	50	50
Z SCORE	Pearson Correlation	-.714**	.977**	1	.546**	-.108
	Sig. (2-tailed)	.000	.000		.000	.456
	N	50	50	50	50	50
VIT_D	Pearson Correlation	-.426**	.529**	.546**	1	-.200
	Sig. (2-tailed)	.002	.000	.000		.164
	N	50	50	50	50	50
DURATION	Pearson Correlation	.063	-.096	-.108	-.200	1
	Sig. (2-tailed)	.665	.505	.456	.164	
	N	50	50	50	50	50

**. Correlation is significant at the 0.01 level (2-tailed).

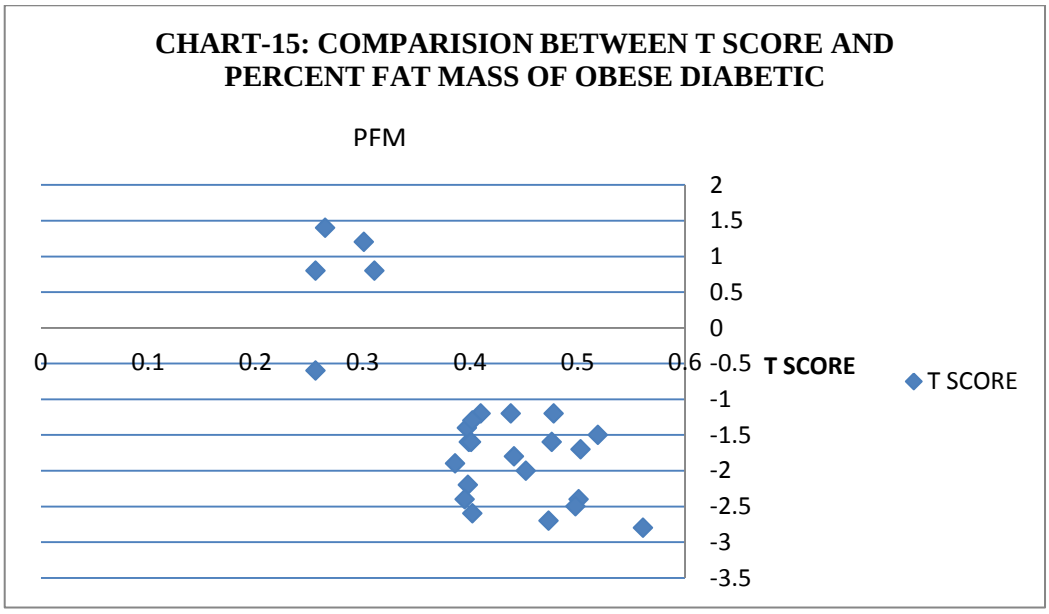
From the above observation with reference to Pearson correlation which signifies an inverse correlation between the body mass index and the T score, Z score, vitamin D levels. All the correlation between these variables is statistically significant with a P value of < 0.05. With reference to Pearson sign which indicates the direction of relation between the variables in which T and Z scores are positively correlated and infact T score acts as a surrogate marker of Z score and viceversa.



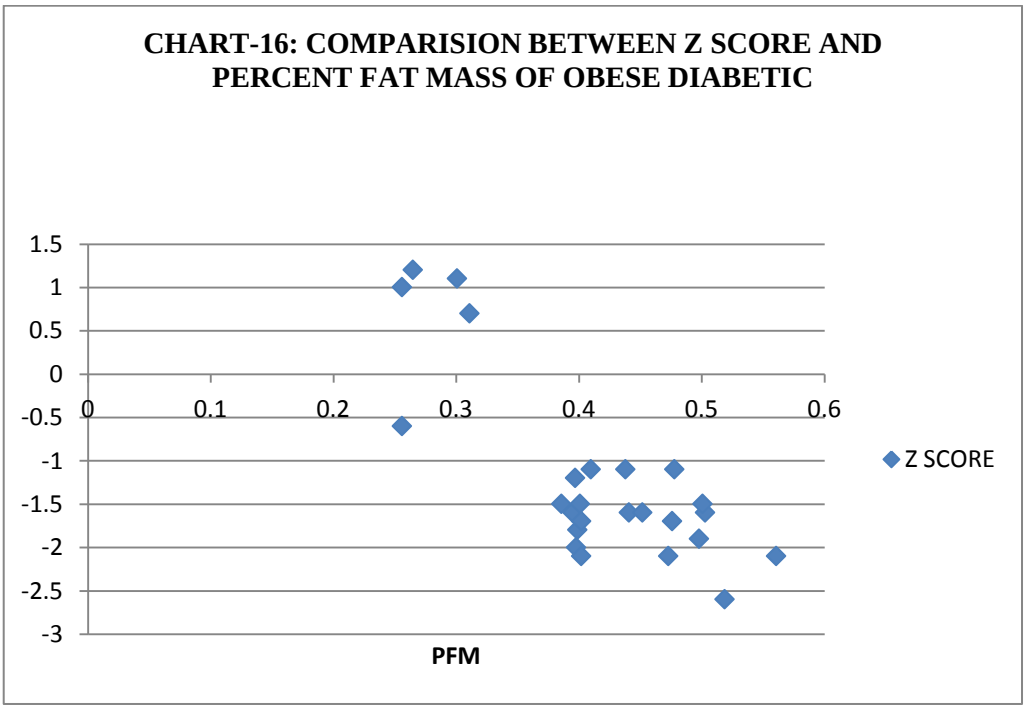
The clustering of T score value between -1.0 to -3 in patients with a BMI of > 30



The clustering of Z score between -1.0 and -2.5 in patients with BMI of > 30



The clustering of T score between 0.4 -0.5 with reference to PFM in obese diabetics.



The clustering of Z score as of T score between0.4 - 0.5with reference to PFM in obese diabetics.

TABLE-13

ANOVA

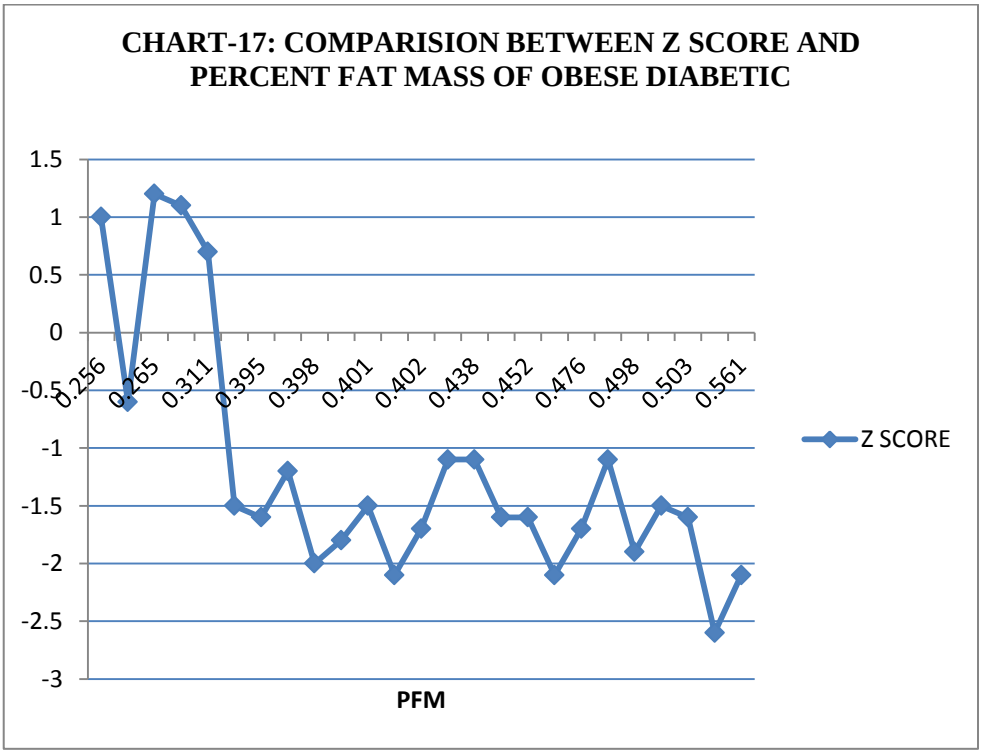
		Sum of Squares	df	Mean Square	F	Sig.
VIT_D	Between Groups	575.236	2	287.618	14.111	.000
	Within Groups	957.953	47	20.382		
	Total	1533.189	49			
BMD	Between Groups	.939	2	.469	34.680	.000
	Within Groups	.636	47	.014		
	Total	1.575	49			

In the analysis of variance in which comparison was made between more than 2 groups the mean vitamin D levels across the groups is statistically significant and significantly different among groups.

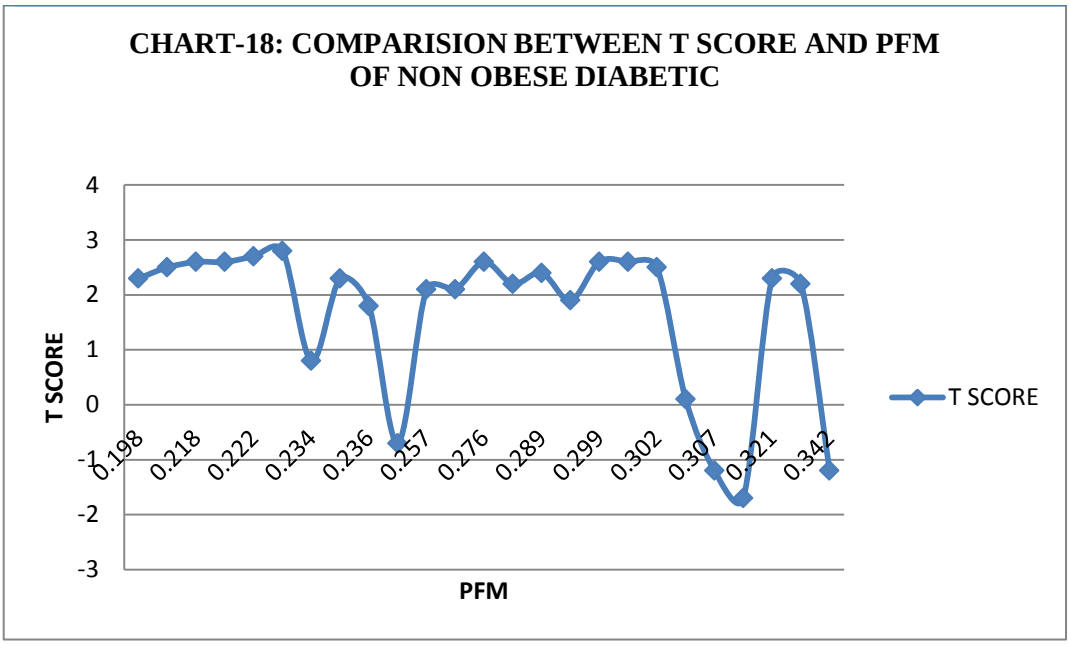
TABLE-14

ANOVA

		Sum of Squares	df	Mean Square	F	Sig.
VIT_D	Between Groups	364.312	2	182.156	7.324	.002
	Within Groups	1168.877	47	24.870		
	Total	1533.189	49			
BMD	Between Groups	.651	2	.326	16.566	.000
	Within Groups	.924	47	.020		
	Total	1.575	49			



Though Z score is not as significant as T score as PFM increases there is increase in negativity of Z score [P<0.05]



The clustering of positivity inT score of non -obese diabetics due to decreased percent fat mass.

DISCUSSION

In our study the prevalence of abnormal bone mineral density among obese diabetics was 80%[cumulative]. Out of which more than 75% with abnormal BMD had osteopenia rather than osteoporosis. Overall the prevalence rate of abnormal BMD in diabetic population with reference to T score is 46% and with reference to Z score is 38%. There was no statistical sex difference in the prevalence of abnormal BMD, as the confounding factors like menopause and other causes of secondary osteoporosis like alcoholism; smoking and systemic disease had been removed.

In accordance with cross sectional studies by Zhao et al and Hsu et al in Chinese population the important observation was that, there was an inverse correlation between the percent fat mass and BMD. In their study they had found out that more the percent fat mass lesser will be the BMD. The difference between their study model and ours was the number of subjects included and they inducted genetic and environmental factors in their study. Ours was an observational study involving a specific subset of a population involving diabetics. The important observation from our study is the relationship between fat mass and obesity is not arbitrary in fact the observation of decreased BMD in obese diabetics when compared to non-obese diabetics who has comparatively normal BMD reiterates the new theory that fat mass is no more protective in fact it is deleterious to

bone health. The average mean Percent fat mass in obese group were 0.417 as compared to 0.268 which is in very much accordance with study by Zhao et al in which they observed PFM is more in obese subjects.

The above observation supports the fact indirectly that larger muscle mass imparts a greater mechanical loading on the skeleton, when this loading effect is removed the net effect of total body fat mass excluding the muscle mass [i.e., lean mass] is detrimental to bone health. In our study by excluding the impact of muscle loading on the skeleton by accounting the percent fat mass which is the ratio of fat mass in grams to total body weight in grams shows an inverse association between BMD and obesity. Hence this observation challenges the concept that obesity is protective against the development of osteoporosis.

Our study did not find any sex difference in the prevalence of abnormal BMD, since the main confounding variable in the female population of our study was menopause which was excluded before inducting the patients in to the study by pre study questionnaire.

In addition we didn't find any correlation between the duration of diabetes and the occurrence of osteopenia or osteoporosis. This finding is in accordance with previous studies from Barret et al [79] who had showed no correlation between the duration of diabetes and abnormality in BMD. We didn't include the glycemic status of the patient in the study as previous studies from Valerio et al [80] and others had clearly showed

no correlation between the glycemic status and abnormal BMD though the pathogenic mechanism behind abnormal BMD in diabetics possibly due to abnormal glycation of type 1 collagen and other proteins may be involved. All of the above mentioned studies had compared the HbA1C levels with lumbar BMD, which they found no correlation. The incidence of fracture rate in study group was only 12%,only two of the patients in the obese group had fracture. One had fracture coccyx and the other patient had fracture of forearm following trauma which was not trivial. The confounding variable for the increased frequency of falls like presence of cataract and peripheral neuropathy was excluded from the study group.

Regarding the influence of diabetes mellitus on bone mineral density various studies had shown contrasting results. A study by petit et al had showed a positive correlation between the BMD and T2DM, in his study he had shown higher BMD in elderly diabetics when compared to age matched non diabetics[81]. This in contrast to study by Yaturu et al in which he had showed a negative correlation between BMD and T2DM in which he had observed lesser BMD in patients with T2DM for age matched normal subjects[82]. In our study we didn't find any correlation between diabetes perse and BMD,because the impact of obesity on BMD had strongly correlated in our study. However the concept that obesity associated with T2DM is protective against the development of osteoporosis is strongly challenged by the fact that in our study group

compromising of obese diabetics out of 25 patients subjected to DEXA imaging 16 of them had osteopenia (64%) and 4 of them had osteoporosis (16%), whereas out of 25 patients in non- diabetic group subjected to DEXA only 3 (6%) of them had osteopenia. These findings are very much in favor of the current prevailing concept that excess fat mass is detrimental to bone homeostasis which is supported by the observation discussed in detail previously that excess adiposity leads to more expression of leptin hormone , which in turn via its central sympathetic effects leads to decrease in bone mineral density.

With reference to vitamin D levels and the body mass index the findings in our study had showed a mean vitamin D levels of 28.427 ng/ml, in patients with adequate bone mineral density. Where as in patients with osteopenia both in obese and non- obese group the mean vitamin D levels were 21.418 ng/ml. This observation was statistically significant [$P < 0.05$]. In patients with osteoporosis the mean vitamin D levels were 23.5 ng/ml .The fact that even though these patients are osteoporotic they had slightly higher vitamin D levels when compared to osteopenic group is probably related to the insufficient number in the osteoporotic group[N=4] . However the important observation in this study is that the mean vitamin D levels in obese population is 23.059 ng/ml, when compared to non- obese group who had a mean vitamin D levels of 27.596 ng/ml is statistically significant[$P<0.05$]. The fact that both these groups are vitamin D insufficient is in accordance with

previous studies in vitamin D in patients with diabetes[84,85]. The increased prevalence of abnormal BMD observed in obese diabetic population is due to increased PFM that has a negative impact on bone rather than due to insufficient levels of vitamin D because both groups had insufficient vitamin D levels but the levels were less in obese diabetics.

The most common pattern of bone mineral density in obese diabetic in this study was osteopenia with a prevalence of 64%. However the prevalence of osteoporosis in obese diabetics was only 16%. Because osteopenia and osteoporosis are continuing spectrum of same disease it is imperative to consider osteopenia is as detrimental as other micro vascular and macro vascular complications of diabetes. There has been no study correlating the pattern of bone mineral density of obese diabetic and non- obese diabetics which, if present will help us to know about the pathophysiology in detail apart from leptin pathway, any other mechanism is involved in the pathogenesis.

Limitations of the study:

- The sample size was small and further studies with larger number of people have to be done to verify the results.

- Since the study was done in ethnic Asian population further studies are needed in large population involving same and different ethnic

group to verify the reproducibility of the results. As most of the reference studies are from Caucasians and Sino Asians.

- Environmental influence on bone health has not been taken in to consideration, as factors like nutrition may affect the bone health adversely.

- Glycemic status has not been taken in to consideration, which may be a possible determinant factor in outcome, though most western studies had not included glycemic status in assessing BMD.

Implications for the future:

- Obesity and diabetes can be included in the screening process for osteoporosis.

- Guidelines for DEXA imaging can be expanded to include diabetics.

- Screening for vitamin D levels is mandatory for all diabetics, as per the WHO guidelines all most all patients in our study were vitamin D insufficient.

- Supplementation of vitamin D may be needed for those patients who are insufficient, even though they are asymptomatic.

- Strict aerobic and weight bearing exercises are advocated for obese diabetics to prevent the detrimental effect of obesity on bone.

- Studies currently available had shown contrasting results between fat and bone this is because of complicated nature of relationship between bone and fat. More studies using molecular and genetic methodology is needed to design an interventional protocol for obesity and osteopenia together.

- Since most of the available studies with reference to obesity and abnormal BMD are cross sectional in nature which has an inherent fallacy in dissecting out the truth, further studies of longitudinal in nature and strong design are essential to find out the true relevance of fat mass on bone homeostasis.

CONCLUSIONS

In our study,

- Obesity is one of the important risk factor for the development of osteopenia inType 2 diabetes mellitus.
- It was observed that percent fat mass was an important factor in predicting abnormal BMD rather than total body weight in obese individual.
- Both android and gynoid fat distribution in excess had negatively correlated with abnormal BMD.
- Vitamin D levels were significantly lowered in obese diabetics when compared to non -obese diabetics though both the group had showed insufficient levels of vitamin D.

Disclosure

The investigator had not received any form of support or grant from any institution or pharmaceutical company.

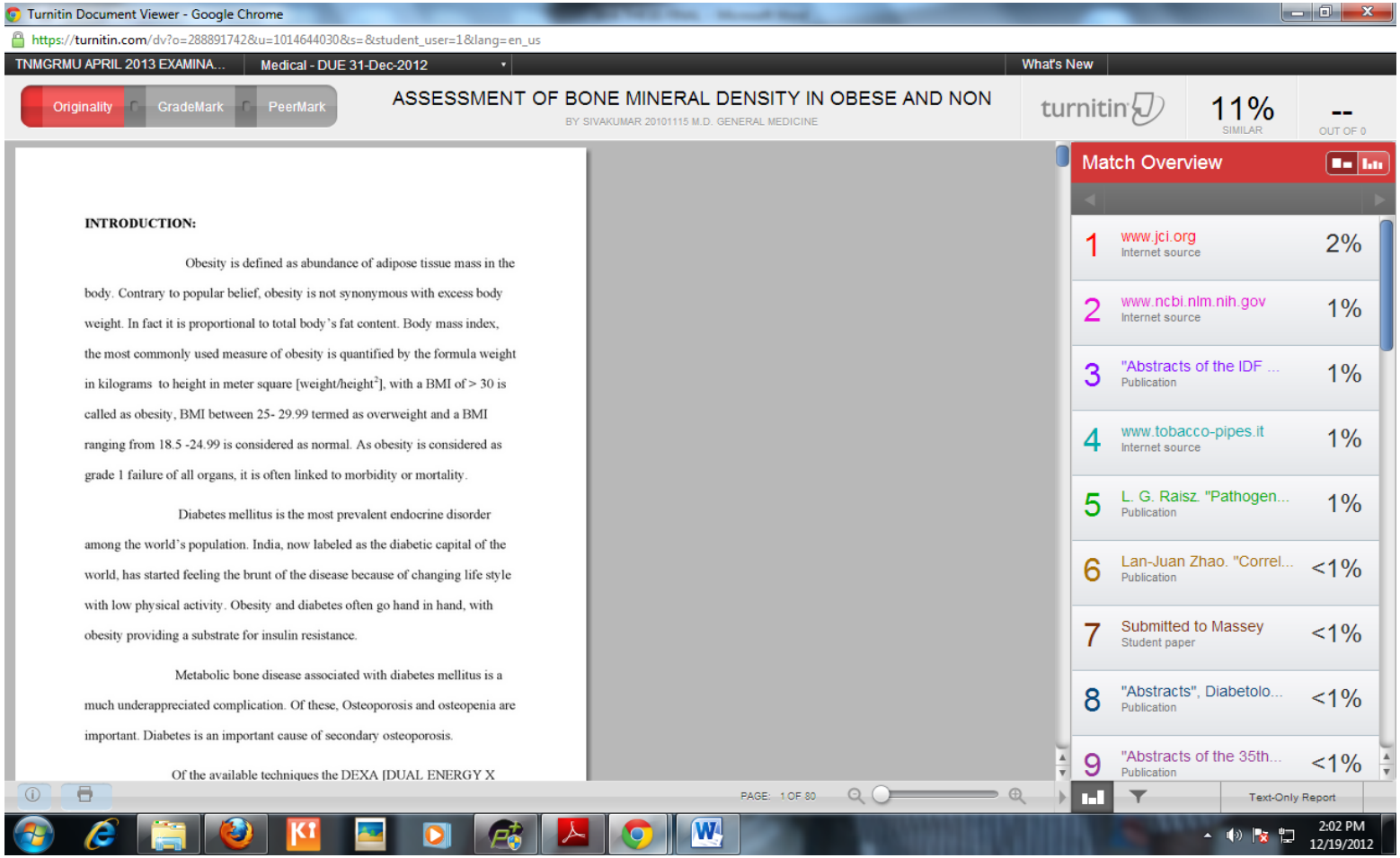
case No	NAME	AGE	SEX	WEIGHT	HEIGHT	BMI	T SCORE	Z SCORE	FAT %	OSTEOPENIA	OSTPOROSIS	MENOPAUSE	DURATION	ETHNIC	OP/IP NO	VIT-D levels	H/O fractures	ANDROID FAT	GYNNOID FAT	BMD g/cm2	PFM
1	MRS.ROOKIAH	45	FEMALE	125.9	155	52.4	-1.5	-2.6	53%	YES	NO	NO	12	ASIAN	6872	21.3	YES	49.1	59.2	1.000	0.519
2	MISS RANI	38	FEMALE	89	168	31.53	-1.6	-1.7	51%	YES	NO	NO	8	ASIAN	7765	20.57	NO	46	42	1.061	0.476
3	MRS.RAJI	40	FEMALE	75	152	32.5	-2.7	-2.1	50%	NO	YES	NO	11	ASIAN	3426	19.6	NO	54.3	53.9	1.198	0.473
4	MRS ERAVAMMAL	46	FEMALE	97	169	33.96	-1.6	-1.5	48%	YES	NO	NO	11	ASIAN	100657	21	NO	48	44	1.296	0.401
5	MR.ABRAHAM	35	MALE	82	160	32.03	-2.2	-2	46%	YES	NO	NA	7	ASIAN	4562	23.4	NO	46.8	45.6	1.257	0.398
6	MR.MUBARAK	40	MALE	75	156	30.81	-1.9	-1.5	41.60 %	YES	NO	NA	3	ASIAN	6456	19.8	YES	49.7	46.7	1.309	0.386
7	MR.NAHOOR	36	MALE	89.7	161	34.6	-1.3	-1.7	42%	YES	NO	NA	7	ASIAN	1034	20.81	NO	49.7	46.7	1.062	0.402
8	MRS.ANDAL	29	FEMALE	78	154	32.8	-0.9	-1.3	39%	NO	NO	NO	7	ASIAN	2341	34.6	NO	43.3	44.7	1.012	0.401

9	MRS.JOTHI	41	FEMALE	68	148	31.04	-1.2	-1.1	41%	YES	NO	NO	13	ASIAN	1789	21	NO	39.7	50.08	1.031	0.438
10	MR.ASLAM	44	MALE	87	163	32.74	-1.8	-1.6	47%	YES	NO	NO	8	ASIAN	1490	22.3	NO	47.6	41.7	1.004	0.441
11	AMBALAVANAR	46	MALE	84	164	31.23	-1.7	-1.6	43%	YES	NO	NO	16	ASIAN	4562	21.4	NO	51.4	41.8	1.012	0.503
12	VENKATESH	37	MALE	78	154	32.88	-2	-1.6	46%	YES	NO	NO	13	ASIAN	6574	20.4	NO	54.3	45.8	0.999	0.452
13	KOTHANDARAMAN	50	MALE	88	165	32.32	-2.4	-1.5	51	YES	NO	NO	16	ASIAN	8934	21.6	NO	63.6	50.9	0.937	0.501
14	PRABHU	34	FEMALE	76	157	30.83	-1.6	-1.8	47%	YES	NO	NO	9	ASIAN	6731	24	NO	50.6	53.6	1.007	0.399
15	VAIRAMUTHU	47	MALE	94	164	34.94	-2.8	-2.1	55%	NO	YES	NO	14	ASIAN	7811	26.7	NO	61.2	54.6	0.879	0.561
16	RANGACHARI	46	MALE	112	162	42.67	-2.5	-1.9	53%	NO	YES	NO	16	ASIAN	111032	22.4	NO	65.4	56.2	0.923	0.498
17	YASIN	47	FEMALE	91	168	32.24	-2.4	-1.6	50%	YES	NO	NO	11	ASIAN	6509	21.4	NO	54.4	53.2	1.002	0.395
18	RANGAN	46	MALE	89	156	36.57	0.8	0.7	48%	NO	NO	NO	13	ASIAN	9084	25.7	NO	48.4	43.7	1.272	0.311

19	VELAMMAL	39	FEMALE	70	140	31.53	1.2	1.1	49%	NO	NO	NO	10	ASIAN	5621	33.2	NO	49	38.3	1.198	0.301
20	JOTHI	42	FEMALE	72	148	32.87	-1.2	-1.1	49%	YES	NO	NO	12	ASIAN	2314	21	NO	49.3	50.8	1.031	0.478
21	ROSALYN	44	FEMALE	76	154	32.04	-1.4	-1.2	53%	YES	NO	NO	15	ASIAN	6723	20.63	NO	56.7	47.3	1.003	0.397
22	DURMA	39	male	82	158	32.84	-1.2	-1.1	48%	YES	NO	NO	10	ASIAN	7612	20.47	NO	53	47.2	1.112	0.41
23	RANI	42	FEMALE	87	167	31.19	0.8	1	47.3	NO	NO	NO	9	ASIAN	7323	22	NO	46	48.5	1.295	0.256
24	KUMARAN	37	MALE	96	172	32.44	1.4	-0.6	47%	NO	NO	NO	8	ASIAN	8943	27	NO	45	49	1.324	0.265
25	HARIKRISHNAN	50	male	102	167	36.57	-2.6	-2.1	57%	NO	YES	NO	12	ASIAN	4319	24.2	NO	56.3	53.2	0.964	0.402

case no	name	age	sex	weight	height	BMI	T score	Z score	fat %	osteopenia	osteoporosis	MENOPUASSE	duration	ethnicity	op/ip NO	VIT D ng/ml	H/O FRACTU	Android obese	GYNEOID OBE	BMD g/cm2	PFM
1	RAMASWAMY	43	male	56	164	20.82	1.8	1.3	33.7	NO	NO	NA	12	ASIAN	5543	22.4	NO	38.5	22.7	1.237	0.236
2	AYYAPAN	46	male	58	167	20.79	2.4	1.8	27.3	NO	NO	NA	8	ASIAN	1784	26.7	NO	33.4	26.7	1.342	0.289
3	MOHAMAD GALINI	47	male	52	154	21.92	2.1	1.4	32.9	NO	NO	NA	11	ASIAN	2907	34.9	NO	35.2	21.7	1.412	0.257
4	GOVARDANAN	39	male	70	170	24.22	2.6	1.8	33	NO	NO	NA	14	ASIAN	2253	37.3	NO	36.7	22.4	1.497	0.301
5	HARIBASKAR	41	male	57	166	20.68	2.2	1.5	29	NO	NO	NA	10	ASIAN	7865	46	NO	38	27	1.489	0.321
6	VENU	40	male	58	161	22.32	2.3	1.8	28.6	NO	NO	NA	13	ASIAN	6745	26.7	NO	33.6	20.6	1.356	0.198
7	NARANGI	36	male	70	174	23.12	2.3	1.6	34.2	NO	NO	NA	7	ASIAN	4589	28.3	NO	32.1	22.7	1.345	0.235
8	SOLAYAPPAN	45	male	57	163	21.45	2.6	1.5	23.7	NO	NO	NA	9	ASIAN	5639	23.2	NO	32.6	22.6	1.321	0.276
9	SOUNDARAPANDIAN	47	male	67	168	23.73	-1.7	-1.6	43.2	YES	NO	NA	13	ASIAN	6783	20.17	NO	36.8	32.6	1.067	0.31
10	JOSEPH MOSES	48	male	66	169	23.1	2.2	1.5	32.3	NO	NO	NA	17	ASIAN	8943	18.98	NO	3.6	32.1	1.387	0.289
11	LINGAPPAN	38	male	50	156	20.54	1.9	1.7	32.7	NO	NO	NA	8	ASIAN	2145	21.56	NO	32.5	18.5	1.476	0.293
12	PERUMAL SWAMY	39	male	59	165	21.67	2.6	2.1	24.7	NO	NO	NA	7	ASIAN	3786	28.9	NO	35.7	21.6	1.421	0.299
13	Lakshmi	37	female	50	156	20.54	0.3	0.8	36.7	NO	NO	NO	11	ASIAN	7893	31.2	NO	42	42.7	1.215	0.34

14	KOTHAI	34	female	61	163	22.95	2.6	2.1	30.5	NO	NO	NO	7	ASIAN	6749	34.1	NO	32.5	23.4	1.342	0.219
15	GEETHA	48	female	51	149	22.97	2.8	2.1	26.9	NO	NO	NO	11	ASIAN	5634	24.6	NO	35.7	32.5	1.442	0.223
16	SEVAMBAL	47	female	62	161	22.77	2.1	1.3	23.6	NO	NO	NO	12	ASIAN	8902	27.8	NO	33.5	36.6	1.267	0.271
17	ARIVUKANNU	43	female	70	169	24.5	2.3	1.6	26.7	NO	NO	NO	13	ASIAN	7865	22.3	YES	34.6	26	1.443	0.321
18	SENTHAMARAI	44	female	54	167	19.36	2.5	2.3	24.2	NO	NO	NO	15	ASIAN	6743	28.6	NO	35.5	26	1.397	0.302
19	ANNAMMAL	41	female	57	163	21.45	-0.7	-0.9	42	NO	NO	NO	13	ASIAN	2214	26.7	NO	36.7	34.6	1.118	0.237
20	CHIMTAMANI	39	female	68	168	24.09	-1.2	-1.5	44.4	YES	NO	NO	15	ASIAN	2300	23.1	NO	33.5	38.6	1.098	0.342
21	FOUZEA MOL	38	female	57	158	22.83	2.5	2.1	27.8	NO	NO	NO	11	ASIAN	4532	33.5	NO	32.3	30.6	1.41	0.217
22	AFSANA	39	female	68	163	21.82	2.7	1.5	26.4	NO	NO	NO	9	ASIAN	2089	29.6	NO	34.5	32.7	1.387	0.222
23	SARAVANI	37	female	61	159	24.12	0.8	0.6	32.5	NO	NO	NO	8	ASIAN	4078	29.4	NO	35.8	36.7	1.143	0.234
24	MYTHILI	46	female	58	155	24.14	-1.2	-1.8	40.7	YES	NO	NO	16	ASIAN	7563	21.6	NO	33.3	37.8	1.087	0.307
25	NELLAIAMMAL	48	female	69	172	23.32	2.6	1.5	33	NO	NO	NO	18	ASIAN	8902	22.3	YES	39.4	32.4	1.345	0.218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INTRODUCTION:
Obesity is defined as abundance of adipose tissue mass in the body. Contrary to popular belief, obesity is not synonymous with excess body weight. In fact it is proportional to total body's fat content. Body mass index, the most commonly used measure of obesity is quantified by the formula weight in kilograms to height in meter square [weight/height^2], with a BMI of > 30 is called as obesity, BMI between 25- 29.99 termed as overweight and a BMI ranging from 18.5 -24.99 is considered as normal. As obesity is considered as grade 1 failure of all organs, it is often linked to morbidity or mortality.
Diabetes mellitus is the most prevalent endocrine disorder among the world's population. India, now labeled as the diabetic capital of the world, has started feeling the brunt of the disease because of changing life style with low physical activity. Obesity and diabetes often go hand in hand, with obesity providing a substrate for insulin resistance.
Metabolic bone disease associated with diabetes mellitus is a much underappreciated complication. Of these, Osteoporosis and osteopenia are important. Diabetes is an important cause of secondary osteoporosis.
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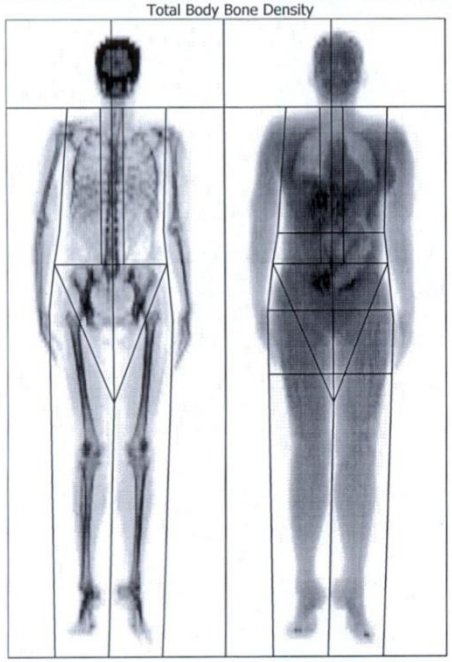
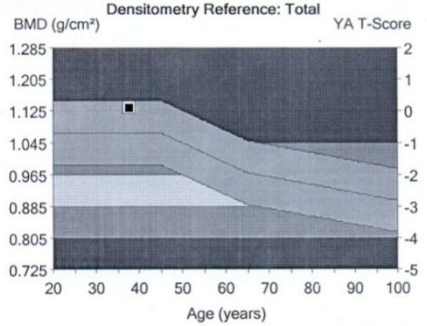
CASE ILLUSTRATION

Patient:	MRS.LAKSHMI,	**Facility ID:**			
Birth Date:	16-Jan-75 37.6 years				
Height / Weight:	156.0 cm 49.2 kg	**Measured:**	04-Sep-12	3:31:29 PM	(11.40)
Sex / Ethnic:	Female Asian	**Analyzed:**	04-Sep-12	3:31:36 PM	(11.40)

Total Body Bone Density



Densitometry Reference: Total



Region	BMD [1] (g/cm²)	Young-Adult [2] T-Score	Age-Matched [3] Z-Score
Total	1.133	0.1	0.8

COMMENTS:

Image not for diagnosis

Printed: 04-Sep-12 3:37:08 PM (11.40)76:0.15:153.04:31.4 0.00:-1.00
4.81x13.01 11.5:%Fat=36.7%
0.00:0.00 0.00:0.00
Filename: owkt9m6gzo.dfb
Scan Mode: Standard 0.4 µGy

1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for Total Body Total)
2 - NHANES (ages 20-30) / USA (ages 20-40) Total Body Reference Population (v110)
3 - Matched for Age, Weight (females 25-100 kg), Ethnic

Patient:	MRS.LAKSHMI,	**Facility ID:**			
Birth Date:	16-Jan-75 37.6 years				
Height / Weight:	156.0 cm 49.2 kg	**Measured:**	04-Sep-12	3:33:12 PM	(11.40)
Sex / Ethnic:	Female Asian	**Analyzed:**	04-Sep-12	3:33:20 PM	(11.40)

DualFemur Bone Density

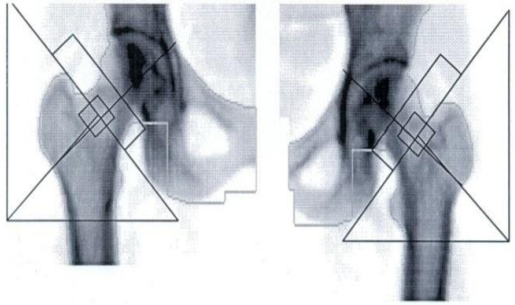
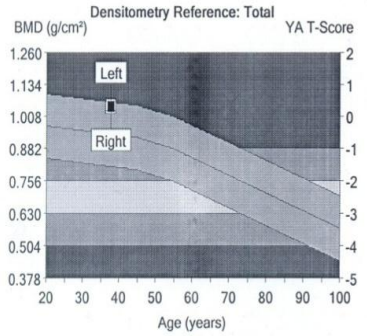


Image not for diagnosis



HAL chart results unavailable

Region	[1] BMD (g/cm²)	[2,7] Young-Adult T-Score	[3] Age-Matched Z-Score
Total			
Left	1.052	0.4	0.9
Right	1.041	0.3	0.8
Mean	1.046	0.3	0.9
Difference	0.011	0.1	0.1

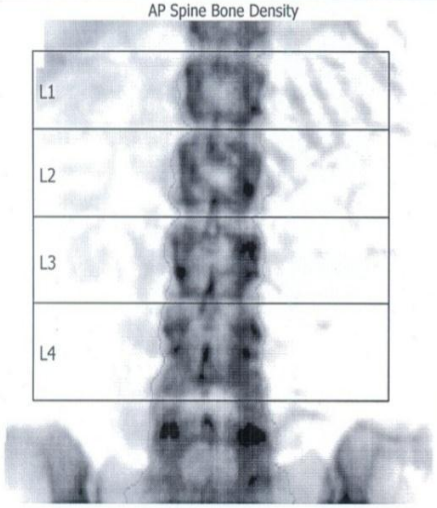
COMMENTS:

1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for DualFemur Total Mean)
2 - NHANES (ages 20-30) / USA (ages 20-40) Femur Reference Population (v110)
3 - Matched for Age, Weight (females 25-100 kg), Ethnic
7 - DualFemur Total Mean T-Score difference is 0.1. Asymmetry is None.
11 - World Health Organization - Definition of Osteoporosis and Osteopenia for Caucasian Women: Normal = T-Score at or above -1.0 SD; Osteopenia = T-Score between -1.0 and -2.5 SD; Osteoporosis = T-Score at or below -2.5 SD; (WHO definitions only apply when a young healthy Caucasian Women reference database is used to determine T-Scores.)

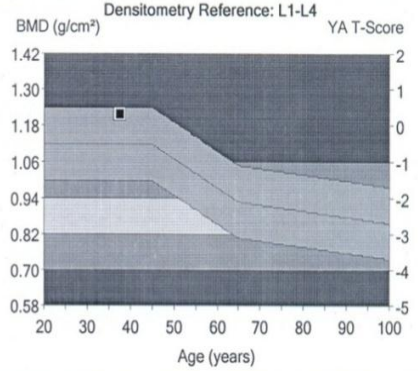
Printed: 04-Sep-12 3:37:25 PM (11.40); Filename: w6lt9m6gzo.dfe; Right Femur; 14.7:%Fat=31.1%; Neck Angle (deg)= 49; Scan Mode: Standard 37.0 µGy; Left Femur; 14.4:%Fat=29.7%; Neck Angle (deg)= 50; Scan Mode: Standard 37.0 µGy

Patient:	MRS.LAKSHMI,	**Facility ID:**			
Birth Date:	16-Jan-75 37.6 years				
Height / Weight:	156.0 cm 49.2 kg	**Measured:**	04-Sep-12	3:34:51 PM	(11.40)
Sex / Ethnic:	Female Asian	**Analyzed:**	04-Sep-12	3:34:58 PM	(11.40)

AP Spine Bone Density



Densitometry Reference: L1-L4



Region	[1] BMD (g/cm²)	[2] Young-Adult T-Score	[3] Age-Matched Z-Score
L1-L4	1.215	0.3	0.8

COMMENTS:

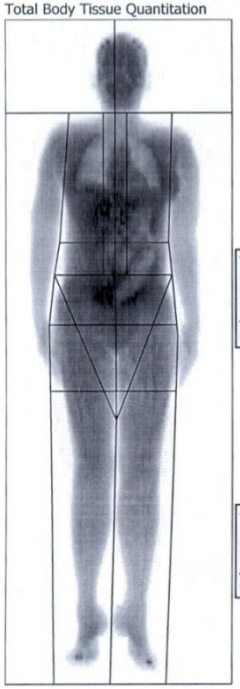
Image not for diagnosis

Printed: 04-Sep-12 3:37:18 PM (11.40)76:3.00:50.03:12.0 0.00:8.88
0.60x1.05 16.4:%Fat=29.9%
0.00:0.00 0.00:0.00
Filename: p9lt9m6gzo.dfs
Scan Mode: Standard 37.0 µGy

1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for AP Spine L1-L4)
2 - NHANES (ages 20-30) / USA (ages 20-40) AP Spine Reference Population (v110)
3 - Matched for Age, Weight (females 25-100 kg), Ethnic
11 - World Health Organization - Definition of Osteoporosis and Osteopenia for Caucasian Women: Normal = T-Score at or above -1.0 SD; Osteopenia = T-Score between -1.0 and -2.5 SD; Osteoporosis = T-Score at or below -2.5 SD; (WHO definitions only apply when a young healthy Caucasian Women reference database is used to determine T-Scores.)

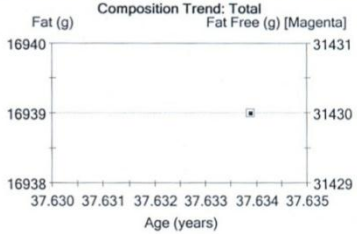
Patient:	MRS.LAKSHMI,		**Facility ID:**			
Birth Date:	16-Jan-75 37.6 years					
Height / Weight:	156.0 cm 49.2 kg		**Measured:**	04-Sep-12	3:31:29 PM	(11.40)
Sex / Ethnic:	Female Asian		**Analyzed:**	04-Sep-12	3:31:36 PM	(11.40)

Total Body Tissue Quantitation



Reference Chart: No reference data for Total Body [Total] region. NHANES/USA Reference Population did not support the patient's ethnicity for Total Body Composition.

Composition Trend: Total



Trend: Total

Measured Date	Age (years)	Tissue[1] (%Fat)	Centile[2,3]	Total Mass (kg)	Region (%Fat)	Tissue[1] (g)	Fat[1] (g)	Lean[1] (g)	BMC (g)	Fat Free (g)
04-Sep-12	37.6	36.7	-	48.4	35.0	46,191	16,939	29,252	2,177	31,430

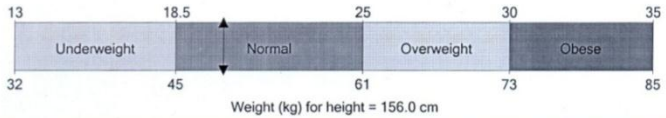
Trend: Fat Distribution

Measured Date	Age (years)	Android (%Fat)	Gynoid (%Fat)	A/G Ratio	Total Body[1] (%Fat)
04-Sep-12	37.6	42.0	42.7	0.98	36.7

COMMENTS:

World Health Organization BMI Classification

BMI = 20.2 (kg/m²)



Weight (kg) for height = 156.0 cm

Image not for diagnosis

Printed: 04-Sep-12 3:37:10 PM (11.40)76:0.15:153.04:31.4 0.00:-1.00
4.81x13.01 11.5:%Fat=36.7%
0.00:0.00 0.00:0.00
Filename: owkt9m6gzo.dfb
Scan Mode: Standard 0.4 µGy

1 -Statistically 68% of repeat scans fall within 1SD (± 0.8 % Fat, ±210 g Tissue Mass, ±520 g Fat Mass, ±610 g Lean Mass for Total Body Total)
2 -USA Total Body Composition Reference Population (v110)
3 -Composition Matched for Age

Patient Name	Mrs. LAKSHMI	Age/ Sex	37/F
Patient ID	/DEXA/02040912	Date	04/09/2012

WHOLE BODY DEXA SCAN

Report:

T- Score of whole body is 0.1

T- Score of left femur is 0.4

T- Score of right femur is 0.3

T- Score of lumbar spine AP is 0.3

Above DEXA features indicate normal bone mineral density.

Whole body fat composition is 36.7 %.

Patient:	MR.NOHOOR MEERAN,	**Facility ID:**			
Birth Date:	23-Jan-77 35.6 years				
Height / Weight:	161.0 cm 89.7 kg	**Measured:**	04-Sep-12	3:53:20 PM	(11.40)
Sex / Ethnic:	Male Asian	**Analyzed:**	04-Sep-12	3:53:28 PM	(11.40)

DualFemur Bone Density

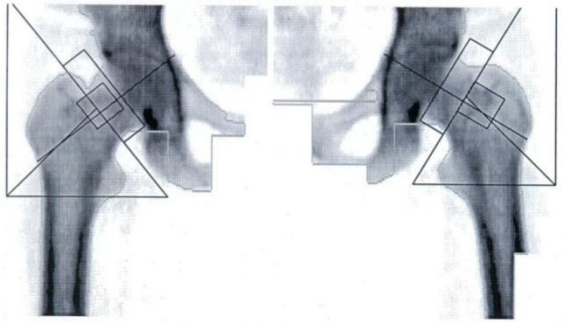
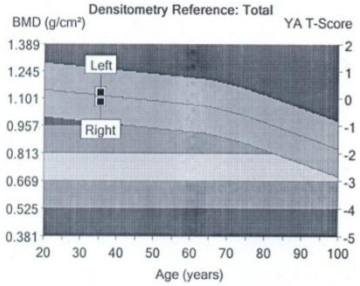


Image not for diagnosis



HAL chart results unavailable

Region	[1] BMD (g/cm²)	[2,7] Young-Adult T-Score	[3] Age-Matched Z-Score
Total			
Left	1.135	0.2	0.1
Right	1.080	-0.1	-0.2
Mean	1.107	0.0	-0.1
Difference	0.055	0.4	0.4

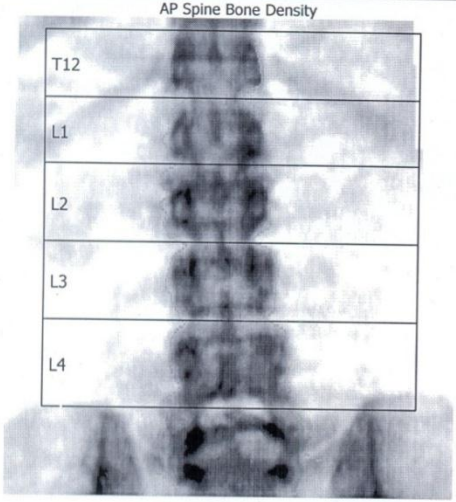
COMMENTS:

1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for DualFemur Total Mean)
2 - NHANES (ages 20-30) / USA (ages 20-40) Femur Reference Population (v110)
3 - Matched for Age, Weight (males 25-100 kg), Ethnic
7 - DualFemur Total Mean T-Score difference is 0.4. Asymmetry is None.
11 - World Health Organization - Definition of Osteoporosis and Osteopenia for Caucasian Women: Normal = T-Score at or above -1.0 SD; Osteopenia = T-Score between -1.0 and -2.5 SD; Osteoporosis = T-Score at or below -2.5 SD; (WHO definitions only apply when a young healthy Caucasian Women reference database is used to determine T-Scores.)

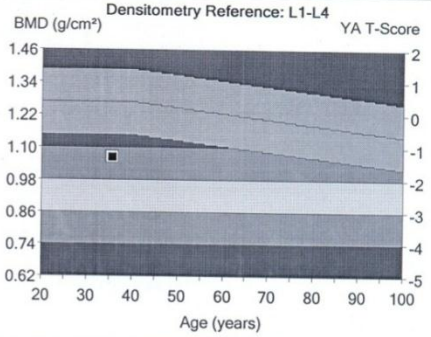
Printed: 04-Sep-12 3:56:07 PM (11.40); Filename: i3mt9m6gzo.dfe; Right Femur; 21.1:%Fat=29.1%; Neck Angle (deg)= 51; Verify there is sufficient pelvis-shaft separation.; Scan Mode: Standard 37.0 µGy; Left Femur; 21.5:%Fat=28.2%; Neck Angle (deg)= 59; Verify there is sufficient pelvis-shaft separation.; Scan Mode: Standard 37.0 µGy

Patient:	MR.NOHOOR MEERAN,	**Facility ID:**	
Birth Date:	23-Jan-77 35.6 years		
Height / Weight:	161.0 cm 89.7 kg	**Measured:**	04-Sep-12 3:55:25 PM (11.40)
Sex / Ethnic:	Male Asian	**Analyzed:**	04-Sep-12 3:55:33 PM (11.40)

AP Spine Bone Density



Densitometry Reference: L1-L4



Region	BMD [1] (g/cm²)	Young-Adult [2] T-Score	Age-Matched [3] Z-Score
L1-L4	1.062	-1.3	-1.7

COMMENTS:

Image not for diagnosis

Printed: 04-Sep-12 3:56:00 PM (11.40)76:3.00:22.24:27.0 0.00:10.92
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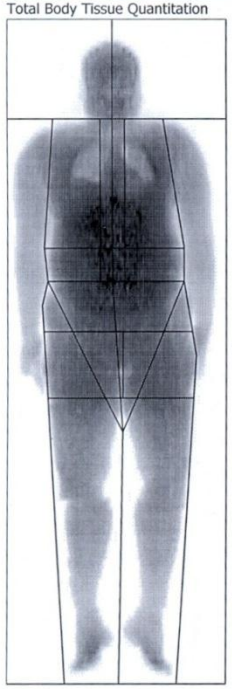
0.00:0.00 0.00:0.00
Filename: c7mt9m6gzo.dfs
Scan Mode: Thick 83.0 µGy

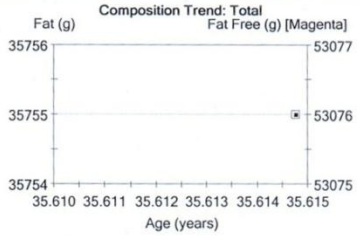
1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for AP Spine L1-L4)
2 - NHANES (ages 20-30) / USA (ages 20-40) AP Spine Reference Population (v110)
3 - Matched for Age, Weight (males 25-100 kg), Ethnic
11 - World Health Organization - Definition of Osteoporosis and Osteopenia for Caucasian Women: Normal = T-Score at or above -1.0 SD; Osteopenia = T-Score between -1.0 and -2.5 SD; Osteoporosis = T-Score at or below -2.5 SD; (WHO definitions only apply when a young healthy Caucasian Women reference database is used to determine T-Scores.)

Patient:	MR.NOHOOR MEERAN,	**Facility ID:**			
Birth Date:	23-Jan-77 35.6 years				
Height / Weight:	161.0 cm 89.7 kg	**Measured:**	04-Sep-12	3:51:02 PM	(11.40)
Sex / Ethnic:	Male Asian	**Analyzed:**	04-Sep-12	3:51:07 PM	(11.40)

Total Body Tissue Quantitation



Reference Chart: No reference data for Total Body [Total] region. NHANES/USA Reference Population did not support the patient's ethnicity for Total Body Composition.



Trend: Total

Measured Date	Age (years)	Tissue[1] (%Fat)	Centile[2,3]	Total Mass (kg)	Region (%Fat)	Tissue[1] (g)	Fat[1] (g)	Lean[1] (g)	BMC (g)	Fat Free (g)
04-Sep-12	35.6	41.6	-	88.8	40.3	86,026	35,755	50,271	2,805	53,076

Trend: Fat Distribution

Measured Date	Age (years)	Android (%Fat)	Gynoid (%Fat)	A/G Ratio	Total Body[1] (%Fat)
04-Sep-12	35.6	49.7	46.7	1.06	41.6

COMMENTS:

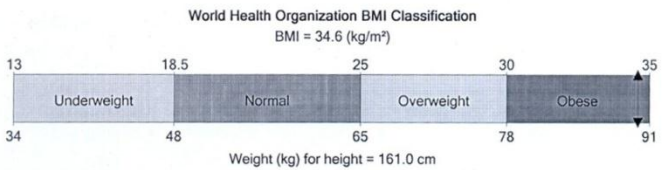


Image not for diagnosis

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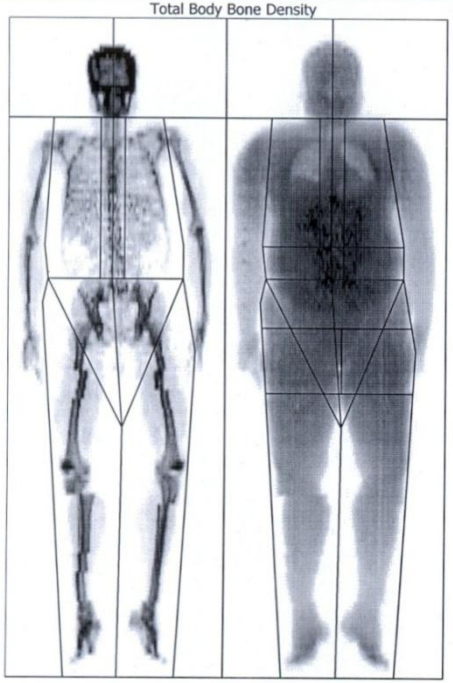
16.0:%Fat=41.6%
0.00:0.00 0.00:0.00
Filename: kolt9m6gzo.dfb
Scan Mode: Thick 0.8 µGy

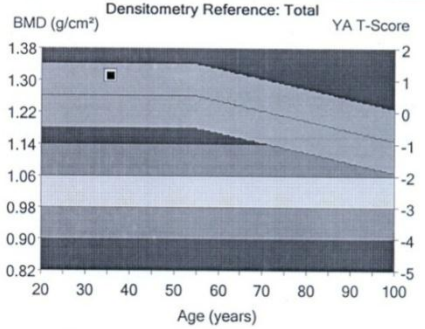
1 -Statistically 68% of repeat scans fall within 1SD (± 0.8 % Fat, ±210 g Tissue Mass, ±520 g Fat Mass, ±610 g Lean Mass for Total Body Total)
2 -USA Total Body Composition Reference Population (v110)
3 -Composition Matched for Age

Patient:	MR.NOHOOR MEERAN,	**Facility ID:**	
Birth Date:	23-Jan-77 35.6 years		
Height / Weight:	161.0 cm 89.7 kg	**Measured:**	04-Sep-12 3:51:02 PM (11.40)
Sex / Ethnic:	Male Asian	**Analyzed:**	04-Sep-12 3:51:07 PM (11.40)

Total Body Bone Density



Densitometry Reference: Total



Region	BMD [1] (g/cm²)	Young-Adult [2] T-Score	Age-Matched [3] Z-Score
Total	1.309	1.1	0.6

COMMENTS:

Image not for diagnosis

Printed: 04-Sep-12 3:56:16 PM (11.40)76:0.15:76.52:62.7 0.00:-1.00
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0.00:0.00 0.00:0.00
Filename: kolt9m6gzo.dfb
Scan Mode: Thick 0.8 µGy

1 -Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for Total Body Total)
2 -NHANES (ages 20-30) / USA (ages 20-40) Total Body Reference Population (v110)
3 -Matched for Age, Weight (males 25-100 kg), Ethnic

Patient Name	Mr. NOHOOR MEEVAN	Age/ Sex	35/M
Patient ID	DEXA/03040912	Date	04/09/2012

WHOLE BODY DEXA SCAN

Report:

T- Score of whole body is 1.1

T- Score of left femur is 0.2

T- Score of right femur is - 0.1

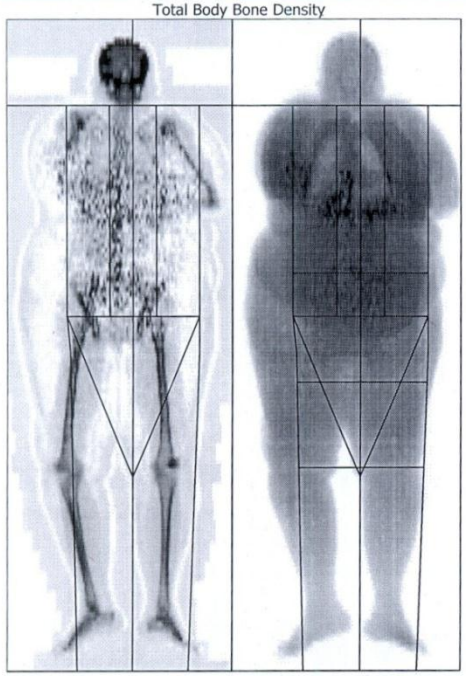
T- Score of lumbar spine AP is - 1.3

Above DEXA features indicate OSTEOPENIA.

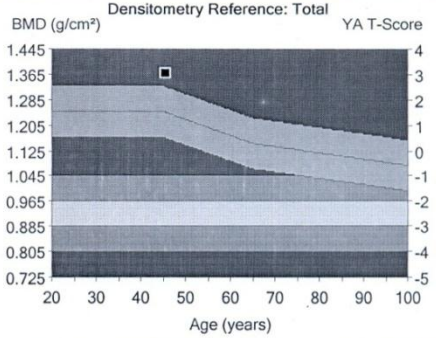
Whole body fat composition is 41.6 %.

Patient:	MRS.ROKIAH BEEVI.,	**Facility ID:**	
Birth Date:	03-Mar-67 45.5 years		
Height / Weight:	155.0 cm 125.9 kg	**Measured:**	17-Sep-12 2:56:04 PM (11.40)
Sex / Ethnic:	Female White	**Analyzed:**	17-Sep-12 2:56:09 PM (11.40)

Total Body Bone Density



Densitometry Reference: Total



Region	[1] BMD (g/cm²)	[2] Young-Adult T-Score	[3] Age-Matched Z-Score
Total	1.367	3.0	1.5

COMMENTS:

Image not for diagnosis

Printed: 17-Sep-12 3:01:47 PM (11.40)76:0.15:76.52:62.7 0.00:-1.00
4.80x13.01 20.8:%Fat=53.0%
0.00:0.00 0.00:0.00
Filename: 6slham6gzo.dfb
Scan Mode: Thick 0.8 µGy

1 -Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for Total Body Total)
2 -NHANES (ages 20-30) / USA (ages 20-40) Total Body Reference Population (v110)
3 -Matched for Age, Weight (females 25-100 kg), Ethnic

Patient:	MRS.ROKIAH BEEVI.,	**Facility ID:**			
Birth Date:	03-Mar-67 45.5 years				
Height / Weight:	155.0 cm 125.9 kg	**Measured:**	17-Sep-12	3:01:10 PM	(11.40)
Sex / Ethnic:	Female White	**Analyzed:**	17-Sep-12	3:01:17 PM	(11.40)

DualFemur Bone Density

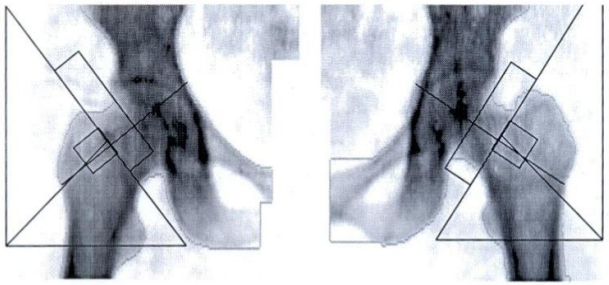
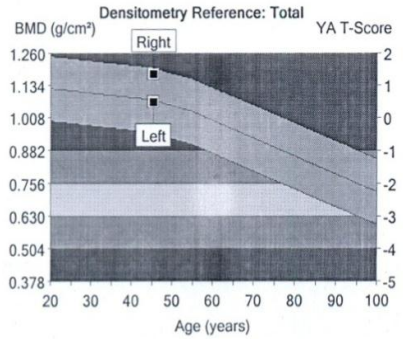
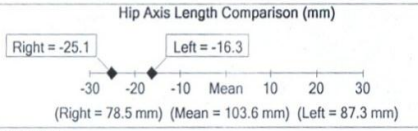


Image not for diagnosis





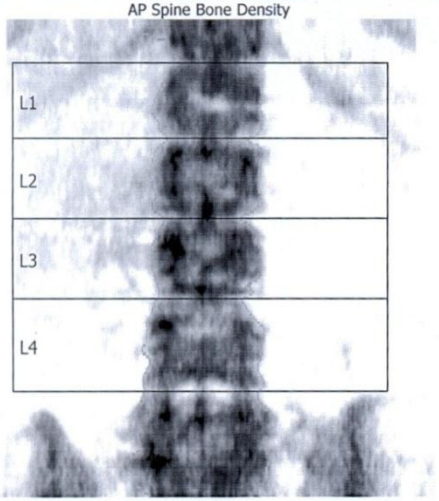
Region	BMD [1] (g/cm²)	Young-Adult [2,7] T-Score	Age-Matched [3] Z-Score
Total			
Left	1.068	0.5	0.0
Right	1.176	1.3	0.8
Mean	1.122	0.9	0.4
Difference	0.108	0.9	0.9

COMMENTS:

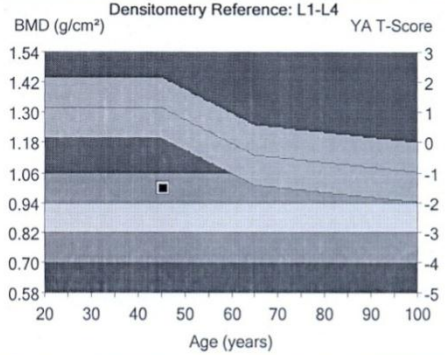
1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for DualFemur Total Mean)

Patient:	MRS.ROKIAH BEEVI.,	**Facility ID:**			
Birth Date:	03-Mar-67 45.5 years				
Height / Weight:	155.0 cm 125.9 kg	**Measured:**	17-Sep-12	2:58:24 PM	(11.40)
Sex / Ethnic:	Female White	**Analyzed:**	17-Sep-12	2:58:31 PM	(11.40)

AP Spine Bone Density



Densitometry Reference: L1-L4



Region	BMD [1] (g/cm²)	Young-Adult [2] T-Score	Age-Matched [3] Z-Score
L1-L4	1.000	-1.5	-2.6

COMMENTS:

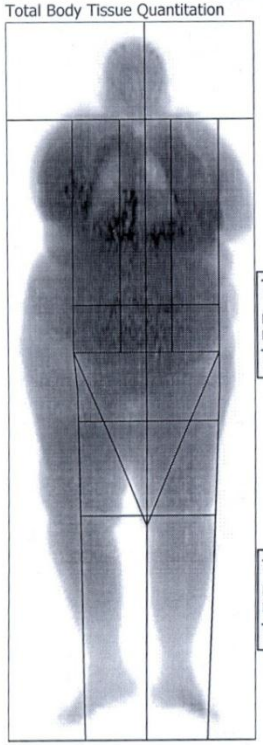
Image not for diagnosis

Printed: 17-Sep-12 3:02:01 PM (11.40)76:3.00:22.24:27.0 0.00:16.50
0.60x1.05 32.0:%Fat=42.6%
0.00:0.00 0.00:0.00
Filename: q7mham6gzo.dfs
Scan Mode: Thick 83.0 µGy

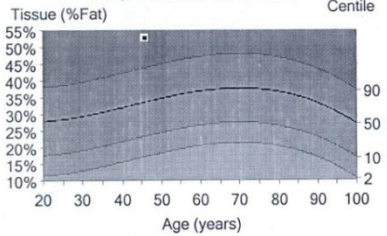
1 - Statistically 68% of repeat scans fall within 1SD (± 0.010 g/cm² for AP Spine L1-L4)
2 - NHANES (ages 20-30) / USA (ages 20-40) AP Spine Reference Population (v110)
3 - Matched for Age, Weight (females 25-100 kg), Ethnic
11 - World Health Organization - Definition of Osteoporosis and Osteopenia for Caucasian Women: Normal = T-Score at or above -1.0 SD; Osteopenia = T-Score between -1.0 and -2.5 SD; Osteoporosis = T-Score at or below -2.5 SD; (WHO definitions only apply when a young healthy Caucasian Women reference database is used to determine T-Scores.)

Patient:	MRS.ROKIAH BEEVI.,	**Facility ID:**	
Birth Date:	03-Mar-67 45.5 years		
Height / Weight:	155.0 cm 125.9 kg	**Measured:**	17-Sep-12 2:56:04 PM (11.40)
Sex / Ethnic:	Female White	**Analyzed:**	17-Sep-12 2:56:09 PM (11.40)

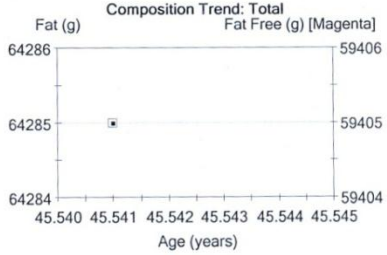
Total Body Tissue Quantitation



Composition Reference: Total



Composition Trend: Total



Trend: Total

Measured Date	Age (years)	Tissue[1] (%Fat)	Centile[2,3]	Total Mass (kg)	Region (%Fat)	Tissue[1] (g)	Fat[1] (g)	Lean[1] (g)	BMC (g)	Fat Free (g)
17-Sep-12	45.5	53.0	99	123.7	52.0	121,396	64,285	57,111	2,295	59,405

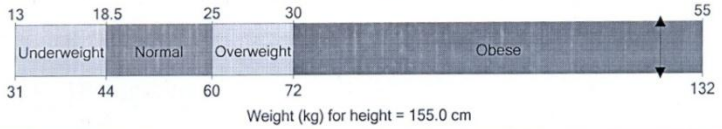
Trend: Fat Distribution

Measured Date	Age (years)	Android (%Fat)	Gynoid (%Fat)	A/G Ratio	Total Body[1] (%Fat)
17-Sep-12	45.5	49.1	59.2	0.83	53.0

COMMENTS:

World Health Organization BMI Classification

BMI = 52.4 (kg/m²)



Weight (kg) for height = 155.0 cm

Image not for diagnosis

Printed: 17-Sep-12 3:01:49 PM (11.40)76:0.15:76.52:62.7 0.00:-1.00 4.80x13.01 20.8:%Fat=53.0%

1 -Statistically 68% of repeat scans fall within 1SD (± 0.8 % Fat, ±210 g Tissue Mass, ±520 g Fat Mass, ±610 g Lean Mass for Total Body Total)

2 -USA Total Body Composition Reference Population (v110)

3 -Composition Matched for Age

Patient Name	Mrs. ROKIAH BEEVI	Age/ Sex	45/F
Patient ID	/DEXA/03170912	Date	17/09/2012

WHOLE BODY DEXA SCAN

Report:

T- Score of whole body is 3.0

T- Score of left femur is 0.5

T- Score of right femur is 1.3

T- Score of lumbar spine AP is-1.5

Above DEXA features indicate OSTEOPENIA

Whole body fat composition is 53.0 %.

LIST OF ABBREVIATIONS USED

PFM	Percent Fat Mass.
FFM	Fat Free Mass.
T2DM	Type 2 Diabetes Mellitus.
T1DM	Type 1 Diabetes Mellitus
BMI	Body mass index.
RANKL	Receptor Activator of Nuclear Factor κβ
NF κβ	Nuclear Factor κβ.
OPG	Osteoprotegerin.
DEXA	Dual Energy X ray Absorptiometry.

VDR	Vitamin D receptor.
M-CSF	Macrophage Colony Stimulating Factor.
ERα	Estrogen receptor α.
TNF-α	Tumor Necrosis Factor – α
LRP5	LDL Receptor related protein 5.
BMP2 .	Bone Morphogenic Protein
COX2	cyclooxygenase 2.
NO	Nitric Oxide.
AGEs	Advanced Glycation End products.

BMD	Bone Mineral Density.

QUESTIONNAIRE

- NAME / AGE / SEX / OCCUPATION / ADDRESS/IP/OP NUMBER.

- HISTORY:

  Onset of diabetes.

  Duration of DM.

  Low back ache.

  H/O Steroid intake.

  Antiepileptic Medications.

  H/O Small and large joint pain.

  H/O Chronic cough.

H/O Tremors.

H/O Chronic diarrohea.

H/O Bilateral feet swelling.

H/O Decreased urine output.

H/O Jaundice.

H/O Numbness of feet, stock and glove pattern of sensory loss.

H/O visual abnormalities.

H/O Loss of weight and appetite.

- PAST HISTORY:

Systemic Hypertension, Dyslipidemia, CAD, CVA, PVD, COPD

and Thyroidal illness, H/O Fractures and site. Past malignancy.

- PERSONAL HISTORY:

Alcohol- Duration , Amount, Frequency. smoking,-Beedi, /cigarette/Number /Day/ Duration.

- MENATURAL HISTORY: Menopause, any other menstrual abnormalities
- DRUG HISTORY:

Calcium, vitamin D supplementation, Oral hypoglycemic agents [pioglitazone] Antihypertensives,Antianginals, Other drugs affecting calcium metabolism.

GENERAL EXAMINATION

VITALS- Blood pressure, Pulse rate.

BMI [Height and Weight]

SYSTEM EXAMINATION: CVS/RS/ABDOMEN/CNS

LOCAL EXAMINATION: Foot ulcers, any joint abnormalities.

- BLOOD SUGAR-FBS/PPBS
- RFT
- LFT
- LIPID PROFILE
- SERUM CALCIUM
- 25(OH)VITAMIN D LEVELS
- CHEST XRAY
- CBC WITH ESR
- DEXA

  AGE

  ETHNICITY

  BMI

  TOTAL FAT PERCENTAGE

TOTAL FAT IN GRAMS

TOTAL BODY MASS IN GRAMS

PERCENT FAT MASS

DIATRIBUTION OF FAT [ANDROID/GYNOID]

T- SCORE- LUMBAR SPINE

Z – SCORE LUMBAR SPINE

BONE MINERAL DENSITY

COMMENTS :

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,CHENNAI-10
Ref.No.6206/MEI(Ethics)/2012 Dt:05.07.2012
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College , Chennai reviewed and discussed the application for approval entitled "A Study on Assessment of bone mineral density in obese & non-obese diabetics by the use of dexa imaging"- For Dissertation Purpose submitted by Dr.K.Sivakumar, MD(GM), PG STUDENT, KILPAUK MEDICAL COLLEGE, CHENNAI-600014.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information / informed consent and asks to be provided a copy of the final report.

GOVT. KILPAUK MEDICAL COLLEGE
14 DEC 2012
Kilpauk, Chennai-10.

14/12/12

CHAIRMAN,
Ethical Committee
Govt. Kilpauk Medical College,
Chennai

TURNITIN ORIGINALITY REPORT

ASSESSMENT OF BONE MINERAL DENSITY IN OBESE AND NON OBESE DIABETICS BY THE USE OF DEXA IMAGING by Sivakumar 20101115 M.D. General Medicine

From Medical (TNMGRMU APRIL 2013 EXAMINATIONS)

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